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**OMNIBUS SOLICITATION OF THE  
NATIONAL INSTITUTES OF HEALTH,  
CENTERS FOR DISEASE CONTROL AND PREVENTION,  
AND FOOD AND DRUG ADMINISTRATION FOR**

**SMALL BUSINESS INNOVATION  
RESEARCH (SBIR)**

**AND**

**SMALL BUSINESS TECHNOLOGY  
TRANSFER (STTR)**

**GRANT APPLICATIONS**

**Part II — NIH, CDC, and FDA Program  
Descriptions and Research Topics**

**RECEIPT DATES**

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**NATIONAL INSTITUTES OF HEALTH**  
April 1, August 1, and December 1, 2003  
(SBIR and STTR)

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**CENTERS FOR DISEASE CONTROL AND PREVENTION**  
April 1 and December 1, 2003  
(SBIR)

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**FOOD AND DRUG ADMINISTRATION**  
April 1, August 1, and December 1, 2003  
(SBIR)

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Part I and Appendices are contained in separate files. Follow the links below to view these documents.

## **PART I – PROGRAM INFORMATION, GRANT APPLICATION INSTRUCTIONS & PREPARATION REQUIREMENTS**

[HTTP://GRANTS.NIH.GOV/GRANTS/FUNDING/SBIRSTTR1/INDEX.PDF](http://grants.nih.gov/grants/funding/sbirsttr1/index.pdf)

## **APPENDICES**

PHS 398 INSTRUCTIONS ([HTML](#) | [PDF VIA FTP](#) | [PDF VIA HTTP](#))

PHS 398 GRANT APPLICATION FORMS – SBIR AND STTR (PHASE I/II) ([PDF](#) | [RTF](#))

SBIR AND STTR REMINDER SHEETS ([PDF](#))

FAST-TRACK SBIR/STTR REMINDER SHEET ([PDF](#))

STTR MODEL AGREEMENT ([RTF](#))

EXTRAMURAL INVENTION REPORTING COMPLIANCE RESPONSIBILITIES ([PDF](#))

ANSWERS TO FREQUENTLY ASKED QUESTIONS ABOUT GRANT APPLICATION FORMAT ([RTF](#))

NIH SBIR/STTR INTERNET GUIDE ([HTML](#))

## PART II – PROGRAM DESCRIPTIONS AND RESEARCH GRANT TOPICS

The research topics shown in this solicitation represent program areas that may be of interest to applicant small business concerns in the development of projects that have potential for commercialization. Small business concerns are encouraged to submit SBIR/STTR grant applications in these areas.

However, SBIR and STTR (applicable to NIH only) grant applications will be accepted and considered in any area within the mission of the awarding components identified in this solicitation.

Applicants are strongly encouraged to query program administrators periodically via email to learn of new or emerging scientific interests of the NIH, CDC, and FDA awarding components.

Additional information on each of the awarding components and their research interests is available electronically on the home pages shown throughout the “Research Topics” section of the solicitation.

The Fogarty International Center, which provides support only for conferences, postdoctoral fellowships for research in the United States and abroad, and senior scientist exchanges between the United States and other countries, does not participate in the SBIR/STTR program.

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### NATIONAL INSTITUTES OF HEALTH (NIH)

The mission of the NIH is to improve human health through biomedical and behavioral research, research training, and communications. The programs of the NIH are oriented principally towards basic and applied scientific inquiry related to the causes, diagnosis, prevention, treatment, and rehabilitation of human diseases and disabilities; the fundamental biological processes of growth, development, and aging; and the biological effects of the environment. In addition, the NIH sponsors training of research personnel; career development of new and established scientists; evaluation and dissemination of new information about medicine and health; construction and renovation of research facilities and provision of other research resources; and improvements in biomedical communications.

To carry out these responsibilities, the NIH is organized into awarding components (Institutes/Centers). Those components that have an extramural element, that is, provide funds for research and research training activities in organizations external to the NIH, are shown below. The NIH makes every effort to finance worthy proposals, including the co-funding of such proposals by one or more awarding components having relevance in the projects.

### TRANS-NIH RESEARCH PROGRAMS

#### Bioengineering Nanotechnology Initiative

See Program Announcement at <http://grants.nih.gov/grants/guide/pa-files/pa-02-125.html>.

The NIH invites grant applications for on nanotechnologies useful to biomedicine. Nanotechnology is defined as the creation of functional materials, devices and systems through control of matter at the scale of 1 to 100 nanometers, and the exploitation of novel properties and phenomena at the same scale. Nanotechnology is emerging as a field critical for enabling essential breakthroughs that may have tremendous potential for affecting biomedicine. Moreover, nanotechnologies developed in the next several years may well form the foundation of significant commercial platforms.

The following list describes some of the priority areas for nanoscience and nanotechnology research support at NIH. The list is not exhaustive, nor are the topics mutually exclusive. Their presentation here exemplifies important scientific areas in which research at the nanoscale has the potential to make enormous contributions to solving biomedical problems.

- A. **Nanomaterials (enabling).** Nano materials science for interfacing with living tissues, passive delivery of pharmaceuticals, tissue engineering scaffolds, contrast and biological agents, and medical devices.
- B. **Nanoimaging.** Real-time subcellular imaging of structure, function, properties and metabolism.
- C. **Cell Biology.** Nano-scale research on cellular processes, including biophysics of molecular assemblies, membranes, organelles, and macromolecules.

- D. **Molecular and Cellular Sensing/ Signaling.** Technologies to detect biological signals and single molecules within and outside cells.
- E. **Nanomotors.** Understanding structure/function and self-assembly; primary and secondary power supply.
- F. **Prosthetics.** Mechanical, chemical, and cellular implant nano-technologies to achieve functional replacement tissue architectures.
- G. **Nanobioprocessor.** Implantable nano scale processors that can integrate with biological pathways and modify biological processes.
- H. **Nanosystem Design and Application.** Fundamental principles and tools to measure and image the biological processes of health and disease; and methods to assemble nanosystems.

Examples of general research topics that would be considered relevant to this trans-NIH initiative include:

- A. Nanoplumbing components such as valves, microfluidic channels, and motors (e.g., to be used as pumps).
- B. Development and improvement of techniques based on new principles for probing biological properties and phenomena not well understood at the nanometer scale and for characterizing nanoscale materials.
- C. Development of fluorescent probes at the nanometer scale for monitoring biochemical processes on the surface and inside a cell in health and disease.
- D. Creation of "smart" nanostructured biocompatible materials. Approaches may include self-assembling techniques and supramolecular chemistry for building up functional nanostructures and for modifying and patterning material surface texture.
- E. Development of nanofabricated barriers to prevent rejection of implantable materials.
- F. Development of nanoparticles and nanospheres that enable controlled release of therapeutic agents, antibodies, genes and vaccines into targeted cells.
- G. Development of sensor technologies for detection and analysis of biologically relevant molecular and physical targets in samples from blood, saliva and other body fluids, or for use in

the research laboratory (purified samples), clinical specimens and in the living body.

### Structural Biology of Membrane Proteins

See Program Announcement at <http://grants.nih.gov/grants/guide/pa-files/PA-02-108.html>.

The NIH invites applications from researchers to solve the structures of membrane proteins at atomic resolution and to develop the tools needed to solve these structures. Considerable research on the structure and function of membrane proteins is under way. Yet, relatively few investigators use x-ray crystallography, electron diffraction, or nuclear magnetic resonance (NMR) spectroscopy to study the structures of these proteins directly. During the past decade, investigators have determined the structures of approximately 30 membrane proteins. The solution of each structure has been a major contribution to a particular area of science (see [http://blanco.biomol.uci.edu/Membrane\\_Proteins\\_xtal.html](http://blanco.biomol.uci.edu/Membrane_Proteins_xtal.html)). This progress clearly demonstrates that determining the structures of membrane proteins is feasible. However, the rate of solving soluble protein structures also has accelerated greatly during the past decade. Thus, a gap remains between understanding membrane proteins and understanding their soluble protein counterparts. The specific objectives of this trans-NIH initiative are to encourage small businesses to: (1) undertake the challenge of solving the structures of membrane proteins, and (2) further develop methods and reagents for studying the structures of membrane proteins at atomic resolution.

Listed below are examples of the types of membrane protein systems that are of particular interest to the participating institutes:

- A. **NIGMS.** Energy transducing membranes of mitochondria, chloroplasts, and bacterial cell membranes involved in electron transport and ATP synthesis; channels, pores, and transporters of ions, substrates, and macromolecules between intracellular compartments and between the cell and its environment; enzymes in the synthesis and metabolism of lipids, membrane-associated and secreted proteins, and glycoconjugates; cytoskeletal proteins, including those required for intracellular vesicle transport, cell motility, and cell division; regulators of cell-cell communication, differentiation, and growth; receptors relevant to cell-cycle regulation,

mechanisms of anesthetic action, and trauma and burn physiology; transporters and enzymes responsible for the uptake, metabolism, and clearance of drugs or other effects on the bioavailability, pharmacokinetics, or action of drugs; targets of drug action and toxicity, including targets of naturally occurring toxins and venoms; and enzymes involved in the biosynthesis of natural products.

- B. **NCI**. Membrane proteins and membrane complexes associated with the biology, diagnosis and treatment of cancer. These include membrane proteins whose alterations have been linked to the development and progression of cancer or that are part of cancer-related signaling pathways; proteins associated with the extracellular matrix (for example, laminins and fibronectin); and proteins with potential as diagnostic markers and/or therapeutic targets. NCI is also soliciting applications focused on the development of new approaches and technologies for the isolation, purification, and structure determination of these proteins. Applicants strictly focused on technology may wish to consider applying under the NCI Innovative Molecular Applications of Technology Program (see <http://otir.nci.nih.gov/tech/funding.html>).
- C. **NIAMS**. Membrane protein systems with specific relevance to muscle function and disease; bone and cartilage function and disease; and skin function and disease. Examples include: membrane proteins involved in excitation, relaxation, force transduction, cellular homeostasis, and metabolism; regulators of cell-cell communication and attachment (e.g., costameres, yotendinous and neuromuscular junctions); ion channels, receptors, transporters, and enzymes that affect the function and hypertrophy or atrophy of muscles; membrane proteins of skin involved in establishment of the stratum corneum barrier, epidermal cell-cell attachment and communication, transmembrane signaling and transport, and cell movement, including genetic and acquired diseases of the skin in which the membrane protein is defective or targeted (which may encompass both benign and malignant hyperproliferative diseases).
- D. **NIDA**. Receptors and transporters relevant to drug abuse research. These proteins include: the cannabinoid CB1 and CB2 receptors; the vanilloid receptor; the orphanin receptor; the

mu, delta, and kappa opioid receptors; the neuronal nicotinic receptor subtypes; the NMDA receptor complex; the metabotropic glutamate receptors I-III; the GABA-A receptor; the dopamine, serotonin, and norepinephrine transporters; and any other neuropeptide receptors that are affected by drugs of abuse.

- E. **NIDCD**. Membrane proteins involved in the auditory, vestibular, olfactory, taste, voice, speech and language sensory systems. Eukaryotic proteins of interest include: transporters, ion channels, ligand receptors, G-protein coupled receptors, transcription and associated factors, motor and motor associated proteins, growth factor receptors, and cytoskeletal structural components involved in the function of these sensory and neural functions. Prokaryotic membrane proteins of interest include: proteins from numerous viral and microbial organisms involved in otitis media or serving as identifiable markers (such as mucin) for middle ear infections.
- F. **NIDDK**. Membrane protein systems with specific relevance to diseases of transport, such as cystic fibrosis and peroxisomal biogenesis disorders; carbohydrate metabolism and its hormonal control; diabetes mellitus; hormone receptors and signal transduction; endocrine disorders; normal and abnormal processes of lipid, protein, amino acid, urea, pyrimidine, metal ion, and steroid metabolism; and genetic metabolic disorders. Proteins should be of mammalian origin. Studies of proteins of prokaryotic or lower eukaryotic origin should be proposed as models for mammalian systems. An example is the ATP Binding Cassette transporter superfamily or traffic ATPases in bacteria and yeast, which serve as models for the cystic fibrosis transmembrane regulator (CFTR).
- G. **NIEHS**. Membrane proteins and enzymes involved in the response of cells to environmental toxicants. These proteins and enzymes may include the components of the stress signaling pathway or ion channels involved in the transport of xenobiotics (e.g., membrane transporters such as PgP, MDR, and MRP2); transporters and enzymes responsible for the uptake and clearance of environmental toxicants; targets of toxicant action, including the Ah receptor and non-classical receptors for endocrine-disrupting agents; and membrane-bound heat shock proteins.



- H. ***NIA, NIMH, and NINDS.*** Neurotransmitter and growth factor receptors, transporters, ion pumps, voltage- and ligand-gated ion channels (e.g., those involved in channelopathy), trafficking proteins, mitochondrial proteins, structural proteins and other proteins involved in the normal function and pathology of cells (neurons and glia) in the central and peripheral nervous systems. Also, proteins involved in synaptic transmission and in the regulation, metabolism, homeostasis, and signaling in the brain during functions such as learning, memory, or cognition, during development and aging into late-life, and in disorders of the central nervous system.
- I. ***NCRR.*** The Biomedical Technology Division is interested the development of new technologies such as instrumentation and methodologies that will enhance the capacity to elucidate structures of membrane proteins.

### **Development of Synthetic and Natural Biomaterial Reference Materials**

The NIH invites applications for the development of synthetic or natural biomaterial reference materials (RMs). RMs are used for standardization of studies of interactions between materials and blood and tissues, for calibration of physicochemical test methods, and/or for reference controls in physical, chemical, and materials structure characterization tests. All innovative developments of biomaterials and devices also need measurements to demonstrate their innovation and improvement. Because RMs lie at the heart of measurement technology, funding for their development could play a key role in future advances in biomaterials and biomedical material device technologies.

Industry uses biomaterial RMs for quality assurance and traceability. The Food and Drug Administration considers them useful for comparing new biomaterials, or new uses of biomaterials, with existing standards and materials. In order to have maximum utilitarian value, it is intended that these biomaterial RMs be stored at, and distributed by, the National Institute of Standards and Technology (NIST). Hence, they must be produced to meet the stringent requirements of the NIST Standard Reference Material Program. *It is important for applicants to contact NIST (Dr. John A. Tesk, (301) 975-6799; Email: john.tesk@nist.gov) to obtain detailed information on requirements of that program prior to preparing and submitting their applications.*

Biomaterial RMs may be synthetic polymers, ceramics, metals, or mixtures of these, or may be derived from living tissues. The choice of RM to be developed is up to the applicant but must be fully justified based on the applicant's knowledge of the magnitude of the current or potential utilization of the biomaterial. RMs of known particular value include: (1) silica-filled poly(dimethylsiloxane), (2) aliphatic polyether urethane, (3) poly(vinylchloride), (4) poly(methylmethacrylate), (5) expanded poly(tetrafluoroethylene) of varying standardized internodal distances, (6) oxygen permeability standards, and (7) carbon materials used in mechanical heart valve designs.

RMs must be of appropriate size and shape. The form in which the reference material is produced and the tests necessary to characterize the material are the decision of the applicant based on the end use of the material. The applicant may consider NIST as a potential subcontractor for measurement and other professional services.

For additional information on this topic, please contact:

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### **National Center on Sleep Disorders Research**

The National Center on Sleep Disorders Research (NCSDR) was established within the National Heart, Lung, and Blood Institute (NHLBI) as a result of the National Institutes of Health (NIH) Revitalization Act of 1993. Its mandate is to conduct and support research, training, health information dissemination, and other activities with respect to sleep disorders, including biological and circadian rhythm research, basic understanding of sleep, chronobiological and other sleep related research and to coordinate the activities of the Center with similar activities of other Federal agencies, including the other agencies of the National Institutes of Health, and similar activities of other public entities and nonprofit entities.

Three specific types of research are emphasized: basic research, using state-of-the-art approaches, to elucidate the functions of sleep and the fundamental molecular and cellular processes underlying sleep; patient-oriented research to understand the cause,

evaluate the scope, and improve the diagnosis and treatment of sleep disorders; and applied research to evaluate the scope and consequences of sleepiness and to develop new approaches to prevent impaired performance during waking hours.

Research opportunities of interest to small businesses may include, but are not limited to, development of:

- A. Advanced, inhome assessment of sleep disturbances and therapeutic effectiveness.
- B. Countermeasures for specific causes of sleepiness, including methods to alter the output of the circadian clock to optimize sleep and wakefulness.
- C. Development of new technologies and instrumentation scaled for high-throughput phenotypic characterization of sleep parameters in mice.
- D. Efficient, objective measures of daytime sleepiness.
- E. Health education methodologies for patients, families, or communities to prevent or cope with sleep disorders or to reduce their impact.
- F. High volume, inexpensive assays for monitoring gene expression in model systems.
- G. Improved methods to diagnose respiratory disorders of sleep in infants, children, and adults.
- H. Interventions to prevent and manage sleepiness to improve productivity and safety.
- I. Methods and techniques to monitor tissue oxygenation.
- J. Methods that will improve patient compliance with treatments for respiratory disorders of sleep.
- K. New therapies for sleep disorders and pharmacological agents to increase alertness.
- L. Noninvasive imaging technologies for evaluating the neurophysiology, regional brain blood flow, and neural pathway changes accompanying sleep and wakefulness.
- M. Novel pharmacological approaches for the treatment of sleep apnea.
- N. Physiological, biochemical, and behavioral assays of sleepiness and methods to monitor levels of alertness continuously and over extended periods of time.

- O. Portable, ambulatory, cost-effective instruments to screen and diagnose sleep disorders.

For additional information on research topics, please contact:

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## NATIONAL INSTITUTE ON AGING (NIA)

The NIA supports biomedical, behavioral, and social research and research training on the aging process as well as on the diseases and other special problems and needs of older people. It supports grant research under four established programs: Biology of Aging, Behavioral and Social Research, Neuroscience and Neuropsychology of Aging, and Geriatrics and Clinical Gerontology.

Examples of research topics within the mission of the NIA that may be of interest to small businesses are shown below. These listings illustrate the range of areas that are of interest to the NIA and are not intended to be exhaustive.

For additional information about areas of interest to the NIA, please visit our home page at <http://www.nia.nih.gov>.

### Biology of Aging

Research on the physiology, molecular, and cellular basis of aging processes. NIA also has responsibility for maintaining existing resources and developing new resources for aging research, such as populations of well-characterized animals and specific cell lines, for example, human fetal lung fibroblasts. Areas that may be of interest to small businesses include, but are not limited to:

- A. Effects of metabolism on the aging process, e.g., how metabolic regulation influences longevity, and the development of anti-oxidant interventions to reduce oxidative stress in vivo.

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- B. Development of minimally-perturbing techniques for collecting blood from mice, rats, and other animals several times a day in sufficient quantities for measurement of hormone levels and other circulating factors in young and old animals, or development of non-invasive research and test methods for use in animals.

Dr. Nancy Nadon  
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- C. Development of molecular probes such as antibodies, DNA sequences and expression vectors useful in studying aging, senescence, and longevity both in vivo and in vitro.

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- D. Instruments and/or methodology to monitor dynamic progression of ovarian follicles from primordial through antral stages in humans and other mammals with sufficient sensitivity to obtain an accurate profile during the perimenopausal period when relatively small numbers of follicles are present.

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- E. Development of new animal models, including transgenic animals, for studying aging processes, as well as development of new biological model systems for research on aging to replace or reduce vertebrate animal use in research. These models may include better in vitro systems, improved cell culture methods, mathematical models, and computer simulations.

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- F. Development of interventions to slow down the degenerative processes associated with aging. These would include techniques with commercial potential to: (1) manipulate the control of cell proliferation or programmed cell death, (2) reduce the level of damage to nucleic acids, proteins and lipids and the macromolecular complexes formed from these molecules, (3) improve the damage surveillance and repair potential of cells, (4)

improve the immune response to foreign molecules or reduce the response to self, and (5) reverse age-related changes in hormone production and function.

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- G. Development of treatments for wound healing in the aged.

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- H. Development of appropriate animal and human culture model systems to explore underlying molecular and cellular mechanisms of prostate growth in middle-aged and older subjects.

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- I. Development of appropriate animal model systems to explore underlying molecular and cellular model systems of female reproductive aging processes as well as the development of pathophysiologic processes associated with the human menopause, including bone loss, cardiovascular pathology, hot flashes, and excessive uterine bleeding.

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## Behavioral and Social Research

Research on basic and translational social and behavioral research on aging processes and the place of older people in society. The program focuses on how people change with age, on the interrelationships between older people and social institutions (e.g., the family, health-care systems), and on the societal impact of the changing age-composition of the population. Emphasis is placed upon the dynamic interplay between the aging of individuals and their changing social and physical environments. Special emphasis areas are Aging Minds (see *The Aging Mind: Opportunities in Cognitive Research*, (<http://books.nap.edu/catalog/9783.html>); Genetics, Behavior and the Social Environment; Health Disparities; Health, Work and Retirement; Increasing Health Expectancy; and Interventions and Behavior Change. Areas that may

be of interest to small businesses include, but are not limited to:

- A. Cognitive and human factors interventions on the individual and environment to maintain independence, maintain functioning, increase well being, and prevent disease/disability. Such interventions can include behavioral technologies, environmental modifications and redesign, training and teaching efforts, or new programs, products and services. Interventions can be developed for home, community, health-care or work-place settings.
  - B. Development of improved technologies for experience sampling methodologies (ESM), which is a method to capture data throughout the day in different environments.
  - C. Social, behavioral, environmental and/or technical interventions on the individual for health maintenance and disease/disability prevention. Such interventions can include self management of chronic diseases including behavioral change technologies, enhancing compliance, especially for less educated patients with chronic diseases requiring strict adherence to complex regimens, or new programs, products and services to increase the health, functioning and well-being of older people. Interventions can be developed for home, community, health-care or work-place settings. Multilevel interventions are especially encouraged.
  - D. AIDS and aging. Development of intervention strategies to prevent the spread of AIDS in middle-aged and older populations. Health education programs to inform the health care providers and public about risks of AIDS in older people.
- Dr. Kathy Mann Koepke  
(301) 402-4156, Fax: (301) 402-0051  
Email: [KoepkeK@nia.nih.gov](mailto:KoepkeK@nia.nih.gov)
- E. Interventions for care provision. Development of strategies for care providers (both professionals and families) to deal with burdens of care associated with chronic disabling illness or disease (including Alzheimer's disease). Interventions include new forms of adult day care, and family interventions. Development of work site programs to supply information on caregiving (including community respite and daycare facilities) and to enable advance planning by employees. Multilevel interventions are especially encouraged.

- F. Elder abuse. Programs and interventions to prevent or reduce elder abuse and neglect in family or community settings and to reduce the susceptibility of older people to crimes, exploitation and victimization.
- G. Death and dying. Programs that deal with decreasing the trauma and difficulty of elders, their families, and care providers in end-of-life decisions and those events that surround the end of life.
- H. Long-term adherence. Development of strategies and technologies to enhance long-term adherence to medical regimes for chronic conditions and behavior-change interventions for health promotion in older adults. Adherence advances might target the healthcare provider, caregiver or patient, or a larger group, such as a social network. Multilevel interventions that have long-term effects are especially encouraged.

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- I. Forecasting. Development of mathematical, economic, demographic and epidemiological models that will lead to improved forecasting of national, state and county level estimates of demand for aging-related services and improved prediction of the effects of public health interventions, changes in health-care financing and insurance, social security, pension coverage or changes in the retirement age. For example, micro- and macro-simulation models of changes in health and economic status and methodological enhancements to existing models that take into account health, intergenerational transfers, changes in family composition, and other characteristics of future cohorts.
- J. Measurement instruments and database support.
  - 1. Development of new instruments using existing demographic and economic data and theory that yield defensible estimates of quality of health plans, hospitals, nursing homes, etc.
  - 2. Development of improved performance-oriented measures of cognitive and physical functioning suitable for use in field settings or in cross-national research.



3. Development of computer-assisted personal and telephone instrument modules, including expert systems, to use with older respondents, in order to determine occupational status, migration, housing issues, disability status, and family structure.
  4. Development of new databases (e.g., from administrative data) and database support to satisfy data and research needs on aging, and innovative data archives and methods for accessing archives to make current statistical and epidemiological data more accessible to researchers.
  5. Development of innovative methods and software to provide improved high performance remote analytic access to complex longitudinal studies or surveys that cannot be placed in open data archives because of issues relating to confidentiality and the need to prevent re-identification of subjects or respondents. Such software would increase the ease with which data analysts could perform sophisticated analyses with a wide range of statistical software programs, while automatically preventing any analyses or remote requests that could compromise data security.
- K. Dissemination and teaching materials. Development of innovative teaching and dissemination tools (e.g., dataset-based computer programs, simulations/games, videotapes and other heuristic devices) to teach dynamics of population aging and convey results of aging research. For example, teaching modules for secondary data analysis for high school and college students using, for example, data from the US Census Bureau, the National Center for Health Statistics, or an NIA sponsored study (see NIA website <http://www.nia.nih.gov/> for available data sets) and projection data.
- L. Interventions on the health-care system. Development and evaluation of strategies to improve health-care organization and delivery including attention to assisted living and new forms of in-home care.

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- M. Development of indicators and measures of progress in the behavioral and social sciences, including bibliometric measures of citations and impact of research, measures of the rate of change and the formation of new research areas, and measures of the impact of behavioral and social research on public policy and well-being.

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- N. Development of miniaturized devices to be used in behavioral and social research to improve real-time, remote monitoring, virtual data collection for instant, continuous, and/or interactive feedback system, and reliable data storage/retrieval.

Ms. Angie Chon-Lee, MPH  
 301-594-5943, Fax: 301 402-0051  
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### Neuroscience and Neuropsychology of Aging

Research on age-related changes in the brain or nervous system in the context of other age-related physiological or homeostatic regulator changes (e.g., endocrine, dietary, immune, disease states); degenerative processes or pathological changes in the aging brain in the context of understanding normal age-related changes; and the sensory, perceptual and cognitive processes and changes that occur with aging as related to their underlying biological mechanisms. An important component of this program is the support of studies on Alzheimer's disease and related dementias of aging. Areas that may be of interest to small businesses include, but are not limited to:

- A. Devices or intervention strategies that may prolong independence when there are dysfunctions of the central nervous system.
- B. Development of sensitive, specific and standardized tests for diagnostic screening of cognitive decline and dementia, for example, the development of biochemical and neuroimaging criteria for the diagnosis of cognitive decline and Alzheimer's disease.
- C. Discovery, development and/or evaluation of drugs, delivery systems, or treatments to enhance cognitive functioning in normal aging and to treat the cognitive deterioration and/or behavioral symptoms associated with Alzheimer's disease as well as to slow and/or

reverse the course of the disease, or prevent it entirely.

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- D. Nutritional interventions to restore brain biochemical changes in aging and neurodegenerative diseases.
- E. Biosensors and prosthetic devices to aid sensory and memory dysfunctions.

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- F. New technologies to screen for the presence of sleep disorders in older persons, to aid in the diagnosis of these disorders, and to enable their remediation.

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- G. Improved instrumentation, imaging technology, related devices, and software packages for use in visualizing neural activity during cognitive or sensory behavior in older adults. Also of interest would be new technologies to combine neural imaging and behavioral assessment in awake unanesthetized animals.

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- H. Development of technology and analysis tools to examine cellular patterns of gene and protein expression in the normal and diseased aging nervous system, including the identification of aberrant gene products expressed in the aging brain. Development of molecular imaging technology for the in vitro and in vivo analysis of gene and protein function in the aging brain.
- I. Development of technology such as non-invasive methods, to identify neural stem cells and to monitor their function in the adult and aged nervous system. Development of novel markers of stem cell proliferation, migration, and differentiation, as well as methods to assess the integration and function of stem cells in the nervous system.

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## Geriatrics and Clinical Gerontology

The Geriatrics and Clinical Gerontology Program supports research on prevention, treatment, and diagnosis of clinical problems that occur predominantly among older persons or that are associated with increased morbidity and mortality in older people; investigations of clinical problems associated with nursing homes and other sites of long-term care for frail older persons. Areas of interest include but are not limited to:

- A. Research on better ways to prevent injuries and deaths associated with the use of currently available bed rails in older patients; this will include improved designs of bed systems for use in the home, nursing home and hospital.
- B. Development of registries and databases on long-lived healthy pairs of relatives or members of families, suitable for use in genetic epidemiologic studies of aging.
- C. Development of vaccines and other agents for preventing and treating infections in older persons, including development of new vaccines or preventive interventions, and new methods using currently available vaccines or preventive medications.
- D. Techniques for preventing or treating urinary incontinence.

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- E. Refinements in techniques for the measurement of age-related changes in hormone levels, status or pharmacokinetics (e.g., those of growth hormone, IGF-1 and its binding proteins; estrogen, progesterone, testosterone; other markers of ovarian, testicular, hypothalamic and pituitary function). The objective is to enhance sensitivity and achieve greater economy in the assay cost.
- F. Effects of menopause on woman's aging and subsequent health. Effects of age-related changes in endocrine status in men on subsequent aging, morbidity and mortality.
  - 1. Refinements in techniques for the measurement of age-related changes in hormone levels or pharmacokinetics (e.g., those of growth hormone, IGF-1 and its binding proteins; estrogen, progesterone,

testosterone; other markers of ovarian, testicular, hypothalamic and pituitary function).

2. Development and testing of alternative strategies (to conventional estrogen/progestin therapy) for the management of short-term menopausal symptoms and for the reduction in risks of cardiovascular disease, osteoporosis, and other menopause-related conditions, disorders and diseases. Development and testing of new tissue-specific modulators of estrogen/androgen receptor activity in men and in women for the prevention or treatment of age-related diseases.
3. Development, testing and validation of new surrogate measures of clinically relevant outcomes and endpoints (e.g., fractures) for (1) more immediate and accurate assessment of the risk or progression of age-related diseases (e.g., osteoporosis) or (2) to predict or monitor efficacy of treatment or enhanced risk or progression of adverse effects/events.
4. Determine drug interactions, i.e., potential alterations in pharmacokinetics and pharmacodynamic properties of drugs taken concomitantly with postmenopausal hormones.

- G. Osteoporosis. Development, testing and validation of new surrogate measures of clinically relevant outcomes and endpoints (e.g., fractures) for (1) more immediate and accurate assessment of the risk or progression of age-related diseases (e.g., osteoporosis) or (2) to predict or monitor efficacy, response to treatment or enhanced risk or progression of adverse effects/events.

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- H. Improved instrumentation (e.g., accelerometers) for assessment of physical activity, and improved monitors for visually and/or biomechanically characterizing falls in older patients.
- I. Improved instrumentation and imaging techniques for measuring body composition and properties such as muscle function in older persons.

- J. Development and validation of non-invasive methods of examining bone quality (density, architecture, and strength of bone).
- K. Development of techniques/devices (e.g., non-invasive, portable) for improved monitoring of caloric intake and/or energy expenditure in epidemiological studies.
- L. Measurement of deficits in muscle strength and balance among older persons.
  1. Instrumentation for biomechanical assessment of ambulation and falls.
  2. Quantitative methods of assessing postural perturbations relevant to activities of daily living.

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- M. Techniques and methods for screening, diagnosis, and treatment of cancer in older persons.
  1. Development of geriatric assessment instruments and/or methodology to assist oncologists in patient evaluation and diagnostic work-up to determine the older patient's overall physical and physiologic health status.
  2. Techniques to promote effective pain management in older-aged cancer patients. This includes documentation and assessment of pain intensity and its characteristics prior to and after pharmacologic and nonpharmacologic interventions.
  3. Development of innovative teaching tools for physicians, nurses, and other health professionals in the following areas: (1) to convey benefits of screening and early detection of cancer for use with older-aged persons; (2) to assist in teaching older-aged patients in self-examination for early warning signs of cancer; and (3) to teach older aged patients how to care for themselves after cancer surgery (e.g., ostomy patients).
  4. Development of methods to be used as guidance for physicians to estimate proper medication dosage in elderly cancer patients given body composition, size, age, other health problems, kidney functioning, and other physiologic parameters. This

includes estimates of an initial or loading dose of therapeutic drugs and daily maintenance for continuance of therapeutic concentration of drugs in the patient's bloodstream.

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- N. Development of devices and techniques for screening substantial numbers of individuals for particular alleles at loci of relevance to human genetic studies of aging.

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### **Other Research Topic(s) Within the Mission of the Institute**

For additional information on research topics, contact:

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For administrative and business management questions, contact:

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### **NATIONAL INSTITUTE ON ALCOHOL ABUSE AND ALCOHOLISM (NIAAA)**

The NIAAA supports research on the causes, prevention, control, and treatment of the major health problems of alcohol abuse, alcoholism, and alcohol-related problems. Through its extramural research programs, the NIAAA funds a wide range of basic and applied research to develop new and/or improved technologies and approaches for increasing the effectiveness of diagnosis, treatment, and prevention. The NIAAA also is concerned with

strengthening research dissemination, scientific communications, public education, and data collection activities in the areas of its research programs.

For additional information about areas of interest to the NIAAA, you are invited to visit our home page at <http://www.niaaa.nih.gov>.

### **Pharmaceutical Development for Alcoholism Treatment**

Applied and, where appropriate, clinical research on pharmacologic agents for use in the treatment or medical management of alcoholism, disorders resulting from alcoholism, the improvement and refinement of drugs currently available for therapeutic purposes, or drugs suitable for use in basic research studies on alcohol addiction. Areas that may be of interest to small businesses include, but are not limited to:

- A. Development of agents to attenuate drinking behavior, e.g., drugs to curb craving.
- B. Development of aversive agents such as disulfiram that attenuate drinking behavior.
- C. Development of agents to treat acute alcohol withdrawal.
- D. Development of agents to treat the protracted withdrawal syndrome.
- E. Development of neurotransmitter agonists and antagonists, or drugs that enhance the efficacy of neurotransmission, which are capable of improving or reversing alcohol-induced cognitive impairments.
- F. Development of agents to induce sobriety in intoxicated individuals (amethystic agents).
- G. Development of agents to diminish drinking by treating associated psychiatric disorders and/or drug abuse.
- H. Development of improved methods of drug delivery for the treatment of alcoholism. The systems developed must be capable of maintaining therapeutic drug levels for extended periods of time to alleviate compliance problems.
- I. Development of drugs for the treatment of alcoholic hepatitis, cirrhosis, pancreatitis, and cardiomyopathy.
- J. Research on the pharmacokinetics of concurrent ethanol and other drug use.



For clinical questions, contact:

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For pre-clinical questions, contact:

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### **Diagnostic Assessment of Alcohol Use Disorders and Comorbidity**

Innovative self-report and biochemical approaches to the early identification of alcohol use problems and diagnosis of alcohol use disorders and comorbidity are needed. The research design should include measurements of reliability and validity in appropriate population samples. Areas that may be of interest to small businesses include, but are not limited to:

- A. Development or adaptation of diagnostic instruments measuring alcohol use disorders and related comorbid conditions in general population and treated samples, including youth, the elderly, pregnant women, ethnic minorities, the handicapped, and persons with low-level reading skills).
- B. Development and testing of methodology to translate diagnostic instruments for alcohol use disorders and associated disabilities into relevant different languages (e.g., various Hispanic languages).
- C. Development and testing of computer algorithms necessary to derive diagnoses of alcohol use disorders and associated comorbidity.
- D. Development of computer software for utilization of assessment instruments in a clinical setting. Development and testing of detailed audio, visual, or printed training modules to accompany diagnostic instruments.
- E. Application of statistical and mathematical analyses to develop models designed to increase our understanding of (1) etiologic relationship between alcohol use disorders and their associated disabilities, and (2) the factors that influence the initiation and maintenance of alcohol use disorders.
- F. Identification, validation, and assay of physiological and/or biochemical measures

capable of identifying individuals at risk for becoming alcoholics or individuals who already exhibit alcohol problems. The accurate measurement of acetaldehyde conjugates or abnormal glycoconjugates in blood is one promising approach.

- G. Development of biochemical/physiological methods for early detection of alcohol-derived pathology, e.g., alcoholic hepatitis or cirrhosis. Development and characterization of markers to accurately predict vulnerability to alcohol-derived pathology.

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### **Treatment of Alcoholism**

- A. Development and evaluation of innovative treatment approaches. These approaches can include outreach, shelter, detoxification, treatment and recovery, and alcohol-free housing, as appropriate.
- B. Development and validation of tools to aid in the clinical management of patients, including selection of appropriate interventions, process evaluation, assessment of outcome, aftercare, and patient tracking, in various treatment settings.

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### **Measurement of Alcohol Consumption/Impairment**

Development of new methods for quantitative measurement of alcohol consumption, development of new and more accurate cost-effective technological approaches for non-invasive measurement of blood alcohol concentration, and development of novel approaches to measure and quantify alcohol-induced impairment of human performance. Areas that may be of interest to small businesses include, but are not limited to:

- A. Development of new methods for quantitatively estimating alcohol use over a period of days or weeks. The approaches should have high sensitivity and specificity and have utility in a variety of settings, including treatment compliance monitoring. Integration of measurement devices with electronic devices

to transmit and/or record data in real time is desirable.

- B. Development of new and more accurate cost-effective technological approaches (such as breathalyzers) for non-invasive measurement of blood alcohol concentration in law enforcement, workplace, research, and clinical settings.
- C. Development of instruments involving tests of behavioral, cognitive, and/or motor function to measure and quantify alcohol-induced impairment of human performance. Such instruments may be computer-based and may be designed to simulate specific work situations such as driving performance, use of complex machinery, learning and retention of new information.

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### **Promoting Adherence to Medical and Behavioral Therapies**

Several recent reports and literature reviews point to the continuing need for improving adherence to therapeutic regimens. Adherence rates vary considerably across diseases and treatments, measuring instruments, and populations, with rates ranging from 30% to 60% in many instances. The reasons for non-adherence are multifaceted. Health-care providers, organizational systems, and personal factors all play a role in adherence to therapeutic regimens. Thus, to understand and eventually improve adherence, conceptual frameworks and interventions need to take into account institutional, system, situational, interpersonal, and personal factors as well as the characteristics of the illness or condition and of the treatment regimen. While extensive research exists and successful techniques have been identified, greater efforts are needed to develop and implement programs based upon these findings. Applications are sought to develop:

- A. Programs to implement effective interventions and to evaluate their implementation.
- B. Professional education courses or web-based training modules on interventions and to monitor their effectiveness.

In both cases, the emphasis is on how to encourage the adoption by health practitioners of interventions

to improve adherence to medical and lifestyle regimens.

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### **Prevention**

Development and evaluation of innovative prevention/intervention programs, or specific materials for integration into existing programs, which utilize state-of-the-art technology and are based on currently accepted clinical and behavioral strategies. Applicants are strongly encouraged to consult with research methodologists and statisticians to ensure that state-of-the-art approaches to design, analysis, and interpretation of studies under this topic are used. Areas that may be of interest to small businesses include, but are not limited to:

- A. Development and evaluation of innovative prevention/intervention programs, or specific materials for integration into existing programs, which utilize state-of-the-art technology and are based on currently accepted clinical and behavioral strategies. Special emphasis should be placed on the needs of high-risk groups, ethnic and minority populations, youth, children of alcoholics, women, the handicapped, and the elderly. Examples of such materials include school-based curricula, interactive videos, computer-based multimedia programs, training manuals for teachers or parents, and community-based programs.
- B. Development and evaluation of educational materials designed to inform the elderly about specific age-related risks for alcohol problems. Particular attention should be given to age-related reductions in alcohol tolerance, interactions between alcohol and prescription and over-the-counter medications, possible exacerbation of some medical conditions common among the elderly, potential biomedical and behavioral consequences of excessive alcohol use, and the role of alcohol in falls, fires, burns, pedestrian and traffic injuries, and other accidents.
- C. Development and evaluation of educational materials designed to provide information on date rape, spouse abuse, child abuse, and other types of violence that have been found to be associated with alcohol use and/or abuse.

The development of strategies for preventing victimization would also be appropriate.

- D. Development of instruments and educational materials designed to improve the effectiveness of employee assistance programs, especially with respect to assessment, referral, and health promotion as it relates to alcohol use and abuse.
- E. Development and evaluation of statistical analysis programs tailored to the design and analysis of alcohol prevention-relevant research. Programs could focus on a variety of areas including: imputation of missing data under varying design assumptions; simulation of distributions of outcomes based on varying mixtures of sample populations; application of chronic or infectious disease models to targeted communities; and models of the potential effect of various policy-based interventions, such as increased taxation or reduction of outlet density by license revocation and control.

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Email: [ksalaita@willco.niaaa.nih.gov](mailto:ksalaita@willco.niaaa.nih.gov)

### Health Services Research on Alcohol-Related Problems

Research projects are sought that will expand knowledge and improve delivery of alcohol treatment and prevention services. The research objectives include, but are not limited to: the effects of organizational structures and financing mechanisms on the availability, accessibility, utilization, delivery, content, quality, outcomes, and costs of alcohol treatment services. Objectives also include studying the effectiveness and cost-effectiveness of alcohol prevention services in reducing the demand for health care services and improving the methodological tools useful for conducting health services research. Areas that may be of interest to small businesses include, but are not limited to:

- A. Development of computer software or other protocols to assist in the management of treatment delivery. Software should be useful for assessment, diagnosis, patient placement criteria, monitoring of services received, tracking patient progress, and billing.
- B. Development of software or other protocols to assist clinicians in scoring and norming results of commonly used assessment instruments.

Output should be in a form useful for guiding client feedback.

- C. Development of software or other protocols to assist treatment programs and service agencies in measuring, assessing, or otherwise documenting indicators of clinical performance or improvements in quality of service provision.
- D. Development of products to facilitate the adoption of evidence-based research findings into everyday clinical practice. For example, training videos or other materials illustrating research-based improvements in treatment practice could provide clinicians with practical examples of orienting patients to pharmacotherapy, assessing motivational readiness, giving motivational feedback, establishing contracts for behavioral couple therapy, and conducting brief interventions in primary care settings.
- E. Development of software or other protocols to facilitate the incorporation of screening and identification tools into routine usage in primary care, emergency, obstetric, mental health, and other health care settings. Research projects should facilitate both the provisions of brief interventions and effective referral to specialized alcohol treatment.
- F. Development of software or other protocols for monitoring clinical costs of alcohol treatment services. These tools should provide a user-friendly system of monitoring costs that could be implemented without additional accounting expertise by the staff at a typical treatment setting. At the same time, such tools should be defensible as measures of the true opportunity costs of providing alcohol treatment services. Such software might be bundled with billing software.

Harold Perl, Ph.D.

(301) 443-0786

Email: [hp14o@nih.gov](mailto:hp14o@nih.gov)

### Training in Alcoholism Assessment and Treatment Techniques

Development of educational materials, including computer-based approaches, for training of health professionals in the use of various assessment techniques and treatment strategies. Areas that may be of interest to small businesses include, but are not limited to:

- A. Development of educational materials, including computer-based approaches, for training of health professionals and paraprofessionals in the use of various assessment techniques and instruments.
- B. Development and evaluation of clinical protocols which enable health professionals to relate assessment to appropriate intervention and treatment strategies.
- C. Development and evaluation of effective health professions training programs which utilize state-of-the-art educational technology and are based upon currently accepted clinical and behavioral strategies. Examples include experiential teaching technologies such as standardized patient, interactive video, and computer simulation.

Cherry Lowman, Ph.D.

(301) 443-0637

Email: [clowman@willco.niaaa.nih.gov](mailto:clowman@willco.niaaa.nih.gov)

### **Fetal Alcohol Syndrome (FAS) and Alcohol-Related Birth Defects**

FAS is a severe developmental disorder that includes mental retardation, cognitive and behavioral disabilities, and motor impairment. The NIAAA supports research leading to improved diagnosis and assessment of impairment and disability, as well as the development of tools to enhance academic and daily living skills. Areas that may be of interest to small businesses include, but are not limited to:

- A. Development of diagnostic and/or screening methods that can be used prenatally to identify fetuses affected by ethanol.
- B. Development and validation of assessment methods to provide more accurate clinical diagnosis of FAS at all life stages.
- C. Development and testing of skill-building, therapeutic, and education program products that enhance the social, cognitive, adaptive and motor abilities of individuals with FAS or fetal alcohol effects.
- D. Development of accurate measures of the responsiveness of children affected by prenatal exposure to alcohol to stress and predictors of vulnerability to alcohol-drinking or other psychopathology during adolescence and adulthood.
- E. Development and evaluation of educational and training programs designed to enhance the

skills of non-professional caregivers in dealing with the problems associated with FAS.

For clinical research questions, contact:

Jan Howard, Ph.D.

(301) 443-1678

Email: [jh184h@nih.gov](mailto:jh184h@nih.gov)

For basic research questions, contact:

Laurie Foudin, Ph.D.

(301) 443-0912

Email: [lf29z@nih.gov](mailto:lf29z@nih.gov)

### **Science Education**

The NIAAA Science Education program is intended to: (1) supplement in-service education of health professionals and paraprofessionals with respect to their recognition and treatment of alcohol-related medical problems; (2) stimulate the interest of both precollege and college students, especially among underserved populations, in career opportunities in the biomedical and behavioral sciences generally and the alcohol field specifically; (3) enhance precollege education in the classroom, both directly and via support to teachers, in the life sciences and in education regarding science-related personal and societal challenges; and (4) improve public understanding of science generally and with particular regard to the role of and need for alcohol research. The NIAAA Science Education program complements, but does not duplicate, the education and training components described under other NIAAA topics.

Efforts in science education might include, but are not limited to:

- A. Development of methodology to transfer new alcohol research knowledge and directions of scientific knowledge growth to curriculum developers and science teachers, consistent with the National Research Council's National Science Education Standards (1996).
- B. Development and testing of specific science education materials, activities or programs to implement one (or more) of the four stated objectives of the NIAAA science education program. The creative use of emerging educational and telecommunications technologies in this regard is of special interest.
- C. Development and testing of methodology to present science and alcohol abuse-related curricula and educational materials to particular



underserved group(s) in culturally relevant ways, and/or to obtain community support for education in science-related and alcohol-related topics that may be culturally sensitive.

- D. Development of resource materials on scientific career opportunities in fields of interest to NIAAA, reflecting activities (e.g., focus groups) and research on motivational factors influencing high school students' career choices, and reflecting economic and social projections of career outlooks for the 21st century.

Peggy Murray, MSW

(301) 443-2594

Email: [pmurray@willco.niaaa.nih.gov](mailto:pmurray@willco.niaaa.nih.gov)

### Longitudinal Analysis of Complex Survey Data

Despite recent advances made in developing software programs for longitudinal latent and observed variable structural modeling, very little has been accomplished in this research arena regarding modeling with complex sample data. Currently there is no comprehensive statistical software package that allows such modeling that takes into account sampling weights, stratification and clustering while at the same time allowing for these observed variables to be either categorical, continuous, or a combination of both. Moreover, there is no currently available comprehensive statistical package that allows for the longitudinal analysis of complex survey data for the variety of models necessary for the analysis of alcohol-related longitudinal data (e.g., linear, probit and logistic regression, survival analysis [continuous and discrete-time allowing for time-varying covariates], path analysis, exploratory and confirmatory factor analysis, growth modeling, growth mixture modeling, multilevel modeling, linear and nonlinear growth modeling, and combinations and variants of these models).

Bridget Grant, Ph.D.

(301) 443-7370

Email: [bgrant@willco.niaaa.nih.gov](mailto:bgrant@willco.niaaa.nih.gov)

### Research Tools

The NIAAA supports basic and applied research to develop new or improved tools to enhance laboratory studies on humans and animals. Examples include transgenic animal models, cell lines, new ligands for neuroimaging, and simulators of alcohol impairment. Areas that may be of interest to small businesses include, but are not limited to:

- A. Development of animal models, including transgenic animals, possessing specific traits of significance for the study of alcoholism, or for the study of specific pathologic disease states which arise from excessive alcohol consumption.
- B. Development of a hepatocyte cell line capable of maintaining viability and metabolic functions in culture systems for an indefinite period.
- C. Development of new methods of ethanol administration to animals that produce precise dose control.
- D. Development of specialized cell culture chambers to provide controlled administration of ethanol to in vitro cell systems.
- E. Development of ligands for alcohol-relevant neurotransmitter systems which will enhance the potential usefulness of PET and SPECT imaging technologies for the study of the etiology of alcoholism and related brain pathology.
- F. Development of instruments that simulate driving, piloting aircraft, or using other complex machinery under hypothetical or actual drinking handicaps and are designed to predict fatal and nonfatal accident involvement.

Laurie Foudin, Ph.D.

(301) 443-0912

Email: [lf29z@nih.gov](mailto:lf29z@nih.gov)

### Other Research Topic(s) Within the Mission of the Institute

For additional information on research topics, contact:

Karen P. Peterson, Ph.D.

Scientific Review Administrator

Extramural Project Review Branch

Office of Scientific Affairs

National Institute on Alcohol Abuse and Alcoholism

6000 Executive Blvd. Suite 409

Bethesda, MD 20892-7003

Phone: (301) 451-3883, Fax: (301) 443-6077

Email: [kpeterso@mail.nih.gov](mailto:kpeterso@mail.nih.gov)

For administrative and business management questions, contact:

Ms. Judy Simons

Grants Management Officer

National Institute on Alcohol Abuse and Alcoholism

Phone: (301) 443-2434, Fax: (301) 443-3891  
 Email: [js182a@nih.gov](mailto:js182a@nih.gov)

## NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES (NIAID)

The NIAID's Division of AIDS, Division of Allergy, Immunology, and Transplantation, and Division of Microbiology and Infectious Diseases fund SBIR/STTR grants on topics related to their mission and activities as described below. Questions on specific research areas may be addressed to the NIAID Program Officials listed below. General questions on the NIAID SBIR programs and on administrative and business management may be addressed to contacts listed at the end of the NIAID section. When possible, applicants are encouraged to use email for communication.

For additional information about areas of interest to the NIAID, please visit our home page at <http://www.niaid.nih.gov>.

### Division of AIDS

The Division of AIDS (DAIDS) supports research on the pathogenesis, natural history, and transmission of HIV and HIV disease, and promotes progress in its detection, treatment, and prevention.

Director: Dr. Ed Tramont  
 (301) 496-0545  
 Email: [et89f@nih.gov](mailto:et89f@nih.gov)

### BIostatistics Research Branch

Statistical methods in HIV studies.

Dr: Dennis O. Dixon  
 (301) 402-2306  
 Email: [dd23a@nih.gov](mailto:dd23a@nih.gov)

### BASIC SCIENCES PROGRAM

Supports basic and applied research on the causes, diagnosis, and prevention of HIV and AIDS.

Associate Director: Dr. Carl Dieffenbach  
 (301) 496-0637  
 Email: [cdd@nih.gov](mailto:cdd@nih.gov)

- A. **Epidemiology Branch.** Population-based research of HIV transmission and associated biological, behavioral, and environmental factors including correlation between immunologic and virologic events and clinical

outcome trends in natural history; correlation between immunologic and virologic events and clinical outcome; and trends in natural history.

Contact: Joana Roe  
 (301) 435-3759  
 Email: [jr108r@nih.gov](mailto:jr108r@nih.gov)

- B. **Pathogenesis Branch.** Molecular and cellular biology, virology, and immunology of virus-host interactions and mechanisms of immunopathogenesis and HIV transmission.

Chief: Dr. Susan Plaeger  
 (301) 402-9444  
 Email: [sp218p@nih.gov](mailto:sp218p@nih.gov)

- C. **Targeted Interventions Branch.** Research areas: (1) targeted therapeutics emphasizing under-explored viral and cellular targets; (2) innovative therapeutic strategies including immune-based and gene-based therapies and therapeutic vaccines; (3) translational research for effective therapeutics spanning preclinical discovery to pilot clinical studies in humans; (4) preclinical discovery and development of topical microbicides and other entities for non-vaccine prevention strategies; and (5) animal models for evaluating new therapeutic entities, regimens, and strategies.

Contact: Dr. Roger Miller  
 (301) 496-6430  
 Email: [rm42i@nih.gov](mailto:rm42i@nih.gov)

### VACCINE AND PREVENTION RESEARCH PROGRAM

Supports the development of vaccines and other biomedical and behavioral interventions to prevent AIDS.

Associate Director: Dr. Margaret (Peggy) Johnston  
 (301) 402-0846  
 Email: [pj7p@nih.gov](mailto:pj7p@nih.gov)

- A. **Vaccine Clinical Development Branch.** Research areas: (1) coordination of phase I, II, and III domestic and international clinical trials of candidate AIDS vaccines; (2) coordination of the characterization of immune responses in HIV-infected and uninfected immunized volunteers; and (3) coordination of studies to identify, validate, and standardize immunologic and virologic markers for monitoring response of participants in vaccine clinical trials.

Chief: Dr. Jorge Flores  
 (301) 496-8200

Email: [jf30t@nih.gov](mailto:jf30t@nih.gov)

- B. **Prevention Science Branch.** Conduct of domestic and international phase I, II, and III clinical trials to evaluate HIV/AIDS prevention strategies, including microbicides, chemoprophylactic agents, and other biomedical and behavioral risk reduction interventions. Basic research on mechanisms of sexual and mother-to-child HIV transmission supportive of new biomedical strategies for interrupting transmission. Translational research on microbicides, spanning preclinical through pilot human clinical research. Pilot clinical studies of the performance of microbicide vehicles and applicators with regard to coverage of and persistence on mucosal surfaces as well as behavioral acceptability.

Chief: Dr. Kevin Ryan

(301) 435-8896

Email: [kryan@niaid.nih.gov](mailto:kryan@niaid.nih.gov)

- C. **Preclinical Research and Development Branch.** Support of applied preclinical development of candidate AIDS vaccines, delivery methods, and adjuvants for the prevention of AIDS; promotion and evaluation of safety and efficacy of the prevention modalities, especially novel vaccine concepts identified in preclinical models including trials in non-human primates; genetic and immunologic variation; and mucosal immunity in SIV, HIV, and SHIV models.

Chief: Dr. James Bradac

(301) 435-3754

Email: [jb68k@nih.gov](mailto:jb68k@nih.gov)

#### THERAPEUTICS RESEARCH PROGRAM

Develops and oversees research and development of therapies for HIV disease, including opportunistic infections (OI) and cancers, in adults, infants, children, and adolescents.

Acting Associate Director: Dr. Frederick Batzold

(301) 496-8210

Email: [fbatzold@niaid.nih.gov](mailto:fbatzold@niaid.nih.gov)

- A. **Clinical Research Management Branch.** Management of grants and contracts supporting therapeutic clinical trials.

Acting Chief: Ms. Margaret Matula

(301) 402-2302

Email: [mmatula@niaid.nih.gov](mailto:mmatula@niaid.nih.gov)

- B. **Drug Development and Clinical Sciences Branch.** Discovery and preclinical development of experimental therapies for HIV, TB and other infectious diseases; maintenance of a database of potential anti-HIV and -OI compounds; immunologic, virologic, and pharmacologic research related to the design and conduct of clinical trials.

Contact: Dr. Chuck Litterst

(301) 402-0132

Email: [cl30x@nih.gov](mailto:cl30x@nih.gov)

- C. **HIV Research Branch.** Clinical research of strategies to treat adult primary HIV infection and complications; strategies to augment HIV immune responses and general host immunity.

Chief: Dr. Carla Pettinelli

(301) 496-0700, Fax: (301) 402-3171

Email: [cp22n@nih.gov](mailto:cp22n@nih.gov)

- D. **Opportunistic Infections Research Branch.** Preclinical and clinical research to develop improved therapies for the treatment and prophylaxis of AIDS-associated opportunistic infections and other complications, including *Pneumocystis carinii* pneumonia, tuberculosis, *Mycobacterium avium* disease, hepatitis C, cryptosporidiosis and *Cryptosporidium parvum* (the microsporidia). Research on metabolic complications of anti-retroviral therapy, emergence of resistance to existing therapies and drug-drug interactions.

Chief: Dr. Barbara Laughon

(301) 402-2304, Fax: (301) 402-3171

Email: [bl17u@nih.gov](mailto:bl17u@nih.gov)

- E. **Pediatric Medicine Branch.** HIV therapies in children and adolescents, strategies to reduce transmission from mother to infant or fetus.

Chief: Dr. James McNamara

(301) 402-2300, Fax: (301) 480-4582

Email: [jm74q@nih.gov](mailto:jm74q@nih.gov)

#### Division of Allergy, Immunology, and Transplantation

The Division of Allergy, Immunology, and Transplantation (DAIT) supports studies of the immune system in health and the cause, pathogenesis, diagnosis, prevention, and treatment of disease caused by immune dysfunction.

Director: Daniel Rotrosen, M.D.

(301) 496-1886

Email: [dr17g@nih.gov](mailto:dr17g@nih.gov)

- A. **Office of Epidemiology and Clinical Trials.** Methodologies to design, manage, and analyze clinical research and epidemiologic research of the etiology, prevention, and treatment of asthma, allergy, and autoimmune diseases.

Director: Ernestine Smartt  
(301) 496-7353, Fax: (301) 402-2571  
Email: [es23r@nih.gov](mailto:es23r@nih.gov)

- B. **Asthma, Allergy, and Inflammation Branch.** Asthma, atopic dermatitis, hypersensitivity reactions, rhinitis, sepsis, sinusitis, urticaria, molecular basis of hypersensitivity, basic studies of asthma and allergy mechanisms, new therapies for asthma and allergic diseases, epidemiology and prevention, phagocyte biology, and mechanisms of host defense.

Section Chief: Dr. Ken Adams  
(301) 496-8973, Fax: (301) 402-2571  
Email: [ka93x@nih.gov](mailto:ka93x@nih.gov)

- C. **Basic Immunology Branch.** Origin, maturation, and interactions of immune cells, immune cell receptors, ligands, and cytokine biology, molecular basis of activation, antigen recognition, tolerance, and immune response regulation, hematopoiesis and stem cell biology, enhancement of vaccine effectiveness in neonates and adults and basic immunology of vaccines.

Chief: Dr. Helen Quill  
(301) 496-7551, Fax: (301) 402-2571  
Email: [hq1t@nih.gov](mailto:hq1t@nih.gov)

- D. **Clinical Immunology Branch.** Autoimmune diseases, primary immune deficiencies (not HIV), basic research of disease mechanisms, immunotherapy of disease processes, disorders mediated by lymphocyte products, and mucosal immunity.

Chief: Dr. Elaine Collier (acting)  
(301) 496-7104, Fax: (301) 402-2571  
Email: [ec5x@nih.gov](mailto:ec5x@nih.gov)

- E. **Transplantation Immunobiology Branch.** Acute and chronic graft rejection, allogeneic and xenogeneic transplantation, development of immunomodulatory agents to prevent and treat graft rejection, genomics of the alloimmune response, hematopoietic stem cell transplantation, major histocompatibility complex, minor histocompatibility antigens,

infectious and malignant complications of immunosuppression in transplantation, technologies for MHC typing.

Chief: Dr. Shiv Prasad  
(301) 496-5598, Fax: (301) 480-0693  
Email: [sprasad@nih.gov](mailto:sprasad@nih.gov)

## **Division of Microbiology and Infectious Diseases**

The Division of Microbiology and Infectious Diseases (DMID) supports research to control diseases caused by all infectious agents, except HIV, through basic investigation of microbial physiology and antigenic structure, pathogenesis, clinical trials of drugs and vaccines, and epidemiologic studies. DMID also supports medical diagnostics research, which is defined as research to improve the quality of patient assessment and care that would result in the implementation of appropriate therapeutic or preventive measures. DMID does not support research directed at the development of environmentally oriented detectors, whose primary purpose is the identification of specific agents in the environment. Note that some of the organisms and toxins listed below are considered NIAID priority pathogens or toxins for biodefense research.

Director: Dr. Carole Heilman  
(301) 496-1884  
Email: [ch25v@nih.gov](mailto:ch25v@nih.gov)

- A. **Bacteriology and Mycology Branch.** Bacteriology and Mycology Branch. Bacterial diseases: anthrax and other zoonotic infections (plague, tularemia, brucellosis, bartonellosis, leptospirosis, glanders), actinomycete infections, enterococcal infections, legionellosis, Lyme disease, melioidosis, nosocomial infections, rickettsial diseases (including *Coxiella*, *Ehrlichia*, and *Rickettsia*), sepsis, staphylococcal infections, urinary tract infections, vector-borne bacterial infections; fungi and fungal diseases: aspergillosis, blastomycosis, candidiasis, coccidioidomycosis, cryptococcosis, histoplasmosis, *Pneumocystis carinii*, other primary and opportunistic fungal infections; antibacterial and antifungal drug resistance; host-pathogen interactions; genetics, molecular, and cell biology; medical bacteriology and mycology; microbial structure and function; development of vaccines, drugs, and medical diagnostics; clinical trials of antibacterial and antifungal agents; and



application of proteomics and genomics to facilitate advances in the areas listed above.

Chief: Dr. Dennis M. Dixon  
(301) 496-7728, Fax: (301) 402-2508  
Email: [dd24a@nih.gov](mailto:dd24a@nih.gov)

**B. Enteric and Hepatic Diseases Branch.**

Research areas: (1) diseases and organisms: astrovirus, Bacteroides, Caliciviruses including Norwalk virus, Campylobacter, Clostridium, Crohn's Disease, diarrhea, enterotoxins, Escherichia coli, gastroduodenal disease, ulcers, gastroenteritis, Guillain-Barré, Helicobacter pylori, Listeria, normal flora, commensals, rotavirus, Salmonella, Shigella, Staphylococcus, Vibrio, Yersinia, Hepatic, hepatitis A, B, C, D, E, G and animal model viruses, transfusion-transmitted virus (TTV), viral hepatitis; (2) basic virology and bacteriology, genome sequencing, natural history and pathogenesis; (3) immunology of infectious diseases including mechanisms of recovery and persistence, protective immune responses and immunopathogenesis in animal models and humans; (4) vaccine research and development to prevent infection and control disease; (5) development and evaluation of adjuvants and vaccine vectors; (6) identification of new drug targets and development and evaluation of drugs; (7) immunotherapy discovery and development; (8) epidemiology, ecology, zoonoses, and transmission; (9) antimicrobial resistance of these organisms in non-nosocomial settings, (10) rapid medical diagnosis and identification of organisms, specific targets, disease, and disease outcome, (11) clinical studies and trials; (12) development of model systems to study infection and disease; and (13) characterization and exploitation of the role of normal flora in disease preventive therapy.

Chief: Dr. Leslye Johnson  
(301) 496-7051, Fax: (301) 402-1456  
Email: [lj7m@nih.gov](mailto:lj7m@nih.gov)

**C. Parasitology and International Programs Branch.**

Research areas: (1) protozoal infections, amebiasis, cryptosporidiosis, cyclosporiasis, giardiasis, leishmaniasis, malaria, trypanosomiasis, toxoplasmosis, Helminth infections, cysticercosis, lymphatic filariasis, schistosomiasis, onchocerciasis, others (e.g., roundworms, tapeworms, and flukes), Invertebrate vectors/ectoparasites, blackflies, mosquitoes, ticks, snails, mites; (2)

parasite biology (genetics, genomics, physiology, and biochemistry); (3) protective immunity, immunopathogenesis, evasion of host responses; (4) clinical and epidemiologic studies of the natural history of tropical and parasitic diseases; (5) research and development of vaccines, drugs, immunotherapeutics, and medical diagnostics, and (6) vector biology and control; mechanisms of pathogen transmission.

Chief: Dr. Michael Gottlieb  
(301) 496-2544, Fax: (301) 402-0659  
Email: [mg35s@nih.gov](mailto:mg35s@nih.gov)

**D. Respiratory Diseases Branch.** Research areas: (1) viral respiratory diseases, including those caused by: coronaviruses, orthomyxoviruses (including influenza A, B and C), and paramyxoviruses (including parainfluenza viruses and respiratory syncytial virus); (2) bacterial respiratory diseases, including those caused by Moraxella catarrhalis (chronic obstructive pulmonary disease), Pseudomonas aeruginosa and Burkholderia cepacia (associated with cystic fibrosis), Corynebacterium diphtheriae (diphtheria), groups A and B streptococci, Haemophilus influenzae, Neisseria meningitidis, Bordetella pertussis (pertussis), Streptococcus pneumoniae, Mycoplasma pneumoniae, Chlamydia pneumoniae and Klebsiella pneumoniae; (3) Otitis media; (4) mycobacterial diseases, including those caused by: M. tuberculosis (tuberculosis), M. leprae (leprosy), and M. ulcerans and other non-tuberculous mycobacterial diseases; (5) development and licensure of vaccines and therapeutic agents for treating and preventing respiratory diseases; (6) maternal immunization; (7) basic research on the pathogenesis, immunity, structural biology, molecular genetics, and genomics of respiratory pathogens; (8) epidemiology and natural history of respiratory pathogens; (9) development of better and more rapid medical diagnostics; and (10) understanding the etiology and long-term health impact of respiratory pathogens in various populations.

Dr. David Klein  
(301) 496-0443, Fax: (301) 402-1456  
Email: [dk27a@nih.gov](mailto:dk27a@nih.gov)

**E. Sexually Transmitted Diseases Branch.**

Development of medical diagnostics, drugs, topical microbicides, and vaccines; role of

STDs in HIV transmission; role of HIV in altering STD natural history; molecular immunology; epidemiologic and behavioral research; adolescents and STDs; STDs and infertility; STDs and adverse outcomes of pregnancy; other sequelae of STDs; Genomics of sexually transmitted pathogens.

Chief : Dr. Carolyn Deal  
(301) 402-0443, Fax: (301) 480-3617  
Email: [cdeal@niaid.nih.gov](mailto:cdeal@niaid.nih.gov)

- F. **Virology Branch.** Acute viral infections and zoonoses, dengue and other arthropod-borne viral diseases (mosquito-borne encephalitis, including West Nile, yellow fever, etc.), hantaviruses, hemorrhagic fevers (Ebola, Lassa, South African hemorrhagic fevers, etc.), measles, polio, coxsackie virus, and other enteroviruses, poxviruses, rabies, rubella; persisting viral diseases and viruses: adenoviruses, bornaviruses, coronaviruses, herpesviruses, parvoviruses, prion diseases; emergence of viral disease; mechanisms of replication, permissiveness, persistence, and latency; vaccines; immune protection and evasion and viral vectors; epidemiology and viral evolution; structure and function of viruses and viral proteins; molecularly targeted approaches to identify and characterize antiviral targets and agents; chemical design and synthesis of novel antiviral agents; in vitro screening and evaluation of antiviral activity; preclinical therapeutic and some prophylactic evaluations of human viral infections in animal models; clinical trials of vaccines and therapies for viral infections; research of civilian defenses for potential bioterrorist use of viruses; and development of rapid medical diagnostic systems.

Chief: Dr. Catherine A. Laughlin  
(301) 496-7459, Fax: (301) 402-0659  
Email: [cl28r@nih.gov](mailto:cl28r@nih.gov)

#### **Other Research Topic(s) Within the Mission of the Institute**

For additional information on research topics, contact:

Dr. Gregory Milman  
National Institute of Allergy and Infectious Diseases  
(301) 496-8666, Fax: (301) 402-0369  
Email: [gmilman@niaid.nih.gov](mailto:gmilman@niaid.nih.gov)

For administrative and business management questions, contact:

Ms. Mary Kirker  
Grants Management Officer  
National Institute of Allergy and Infectious Diseases  
(301) 496-7075, Fax: (301) 480-3780  
Email: [mk35h@nih.gov](mailto:mk35h@nih.gov)

#### **NATIONAL INSTITUTE OF ARTHRITIS AND MUSCULOSKELETAL AND SKIN DISEASES (NIAMS)**

The NIAMS supports research in arthritis and musculoskeletal and skin diseases. Such research is directed at basic understanding of the causes and development of rheumatic diseases, connective tissue diseases, musculoskeletal and skin disorders and diseases. Basic investigations involve immunology; purine metabolism; skeletal muscle structure, function, metabolism and physiology; the structure, function, production, biochemistry and physiology of collagen, elastin, and other proteins of connective tissue; metabolic and hormonal changes in bone; prevention and treatment strategies for osteoporosis and related bone diseases, structural and biochemical changes in osteoarthritic cartilage and cartilage repair; novel imaging modalities for bone, cartilage, and connective tissues; new treatments for fractures and other musculoskeletal tissues including tissue engineering and gene therapy; orthopaedic implant science (materials, design, wear, osteointegration); bioimaging of musculoskeletal tissues; computer-assisted orthopaedic surgery and other computer-assisted musculoskeletal bioimaging and treatment interventions; the biomechanics of normal, arthritic and prosthetic joints; the structure, function, barrier properties, metabolism, and physiology of the skin. Exercise research related to musculoskeletal function, including the development of tools or behavior modification programs to enhance exercise in normal individuals or those with chronic diseases, and related behavioral and prevention research.

For additional information about areas of interest to the NIAMS, please visit our home page at <http://www.niams.nih.gov>.

#### **Arthritis and Musculoskeletal and Skin Diseases**

- A. **Rheumatic Diseases Branch.** Supports basic and clinical research in the normal function and components of connective tissue and the immune system and their dysregulation in

rheumatic, genetic, and inherited diseases of connective tissue. The goals are increased understanding of the etiology and pathogenetic mechanisms involved in rheumatic and degenerative disease of the joints and in the translation of these basic research findings to prevention, diagnosis, and treatment of disease. The research supported by the Program utilizes approaches emanating from relevant areas of genetics, biochemistry, cellular and molecular biology, biophysics, enzymology, immunology, pathology, physiology, behavioral medicine, and epidemiology.

A description of other areas of research under investigation may be found at <http://www.niams.nih.gov/rtac/funding/grants/ep3.htm>.

- B. **Musculoskeletal Diseases Branch.** Supports studies of the skeleton and associated connective tissues. Research areas supported through the Musculoskeletal Diseases Branch include bone diseases, bone biology, and orthopaedic research. Broad areas of interest include skeletal development, metabolism, mechanical properties, and responses to injury. Osteoporosis, a disease afflicting many of the Nation's growing population of older people, is particularly emphasized for investigation under this program. Among other diseases and skeletal disorders under investigation are osteogenesis imperfecta, a genetic disorder that leads to fragile, easily fractured bones; Paget's disease of bone, which results in irregular bone formation and subsequent deformity; genetic disorders of bone growth and development, such as osteopetrosis and the osteochondrodysplasias; vitamin D refractory diseases; and rickets and osteomalacia. Other studies focus on the causes and treatment of acute and chronic injuries, including carpal tunnel syndrome, repetitive stress injury, low back pain and clinical and epidemiological studies of osteoarthritis. The Program supports development of new technologies with the potential to improve treatment of skeletal disorders and facilitate the repair of trauma in the normal skeleton. These include drugs and nutritional interventions, joint replacement, bone and cartilage transplantation, and gene therapy. In addition, bioengineering, sports medicine and musculoskeletal fitness are areas of special research emphasis.

A description of other areas of research under investigation may be found at <http://www.niams.nih.gov/rtac/funding/grants/ep5.htm>.

- C. **Skin Diseases Branch.** Supports basic and clinical studies of the skin in normal and disease states. The wide range of skin diseases under study with NIAMS support includes keratinizing disorders such as psoriasis and ichthyosis, atopic dermatitis and other chronic inflammatory skin disorders, the vesiculobullous diseases such as epidermolysis bullosa and pemphigus, acne, and vitiligo.

A description of other areas of research under investigation may be found at: <http://www.niams.nih.gov/rtac/funding/grants/ep6.htm>.

1. Determinations of drug effects.
2. Determinations of effects of other therapies, including occupational and physical therapy modalities, spinal manipulation, bracing, transcutaneous nerve stimulation, acupuncture, and topical agents (e.g., capsaicin).
3. Preventive strategies.
4. Development and validation of animal models for rheumatic, musculoskeletal (especially for herniated intervertebral disc and spinal stenosis), muscle and skin diseases.
5. Improvement and refinement of immunogenetic determinants of rheumatic diseases.
6. Development of novel and improved diagnostic methods and treatments for muscle, tendon, ligament, bone, and joint injuries, including overuse and repetitive motion disorders.
7. Devices and activities designed to prevent muscle, tendon, ligament, and joint injuries, including overuse and repetitive motion disorders.
8. Assessment techniques for musculoskeletal and skin diseases.
9. Functional and metabolic measures of the musculoskeletal system in normal, diseased and active states.
10. Development of novel implant designs, materials and surface coatings for

- musculoskeletal implants. Development of assessment strategies to detect implant failure, loosening, and osteolysis, and the development of novel technologies to prevent them.
11. Computer modeling, relevance to the musculoskeletal system.
  12. Improved topical treatments of skin diseases and disorders.
  13. Devices and computer programs for diagnosis or assessment of skin diseases.
  14. Tissue culture models for skin diseases.
  15. Artificial skin.
  16. Photoprotective agents.
  17. Improved treatment for bone diseases.
  18. Measurement techniques for bone diseases.
  19. Preventive measures for fractures.
  20. Delivery systems for dietary supplements.
  21. Novel delivery systems for therapeutic agents.
  22. Development of novel or improved technologies for bone healing and repair. This includes, but is not limited to, the development of osteoinductive, osteoconductive, or a combination, technologies to facilitate bone healing/repair, and the development of improved or novel approaches to the use of autogenous, allograft, and bone graft substitutes.
  23. Development of novel or improved technologies to facilitate the repair of articular cartilage, including, but not limited to cartilage cell transplantation, use of stem cells, biodegradable scaffolds, growth factors, and refinements of currently existing technologies.
  24. Development of novel technologies to improve the diagnosis, prevention, and treatment of acute and chronic low back pain.
  25. Development of novel assessment technologies for identifying biomechanical inputs on bone and cartilage tissue at the cellular level, and identification of the corresponding physiological response.

26. Development of novel technologies leading to the use of gene therapy for selected musculoskeletal diseases and injuries.
27. Development of novel, non-invasive technologies to assess joint tissues, including articular cartilage and subchondral bone.

### Markers of Osteoarthritis

The NIAMS seeks applications for the development and validation of standardized, sensitive assays for osteoarthritis markers in body fluids or tissue specimens. Osteoarthritis is the most prevalent musculoskeletal disorder, characterized by joint pain, tenderness, and functional disability. The percentage of Americans over 65 years of age is the fastest growing segment of the population, which is expected to reach 68 million people by the year 2010. A biochemical test for osteoarthritis would be particularly useful for early detection, assessment of disease severity and progression, and to monitor the effects of therapies.

Advances in the molecular biology, biochemistry, and metabolism of cartilage have stimulated the quest for appropriate markers of degradative and regenerative processes in osteoarthritis. Important new studies indicate that molecular fragments of cartilage-derived matrix molecules are present in the blood and joint fluid in osteoarthritis that have the potential to represent disease-specific markers. The increased rates of cartilage degeneration increase the concentration of matrix components in tissue and body fluids, thus reflecting changes in the rates of cartilage catabolism. Further, cartilage degeneration in osteoarthritis changes the type or structure of the molecules being synthesized by the chondrocytes. Thus, the presence of these neo-epitopes may be a marker of degenerative events within the tissue. Markers of metabolic changes in subchondral bone or other joint tissues in osteoarthritis are also of potential interest.

The NIAMS is soliciting applications to test the potential application of a marker for osteoarthritis diagnosis, prognosis or severity and the standardization of a clinically relevant test. Successful applicants will provide a rational approach for the development of a practical and reliable assay for osteoarthritis disease marker(s) and determination of the sensitivity and specificity of the marker(s) in patient populations. The applications must include the rationale for the selection of the marker to be employed in the study.

If a battery of markers will be utilized the basis of this approach must be clear and well justified. The assay systems as well as the methods of sample collection, storage, and handling must be clearly delineated. Marker levels must be validated against other methods of monitoring osteoarthritis, such as imaging techniques. The expected outcome of these studies is an osteoarthritis test that can be used in larger scale human trials.

### **Muscle Biology, Exercise Physiology and Sports Medicine**

A. **Muscle Biology Branch.** Supports research on skeletal muscle, its diseases and disorders, and its central role in human physiology and exercise. Topics include the molecular structure of muscle and the molecular mechanisms that produce force and motion. An aim is understanding the alterations in muscle resulting from increased exercise regimens and, conversely, the atrophy that follows immobilization during injury or illness. Some of the specific areas of research covered by the Muscle Biology Branch include Muscle Physiology, Molecular Architecture, Muscle Membranes, Muscle Development and Specialization, Musculoskeletal Fitness and Adaptive Biology, Muscle Diseases, and Sports Medicine, Muscle Injury and Muscle Repair. Areas that may be of interest to small businesses include but are not limited to:

#### **1. Muscle Structure and Function.**

Research on the application of biochemistry, molecular, and cell biology to muscle biology, including studies of membrane structure, function, and biosynthesis, lipid metabolism, membrane models, membrane transport, sub-cellular organization, organelles, cytoskeletal components, and cell division. Development of new instruments and methods to facilitate studies on muscle function and physiology. Specific examples might include, but are not limited to, the following:

- a. Development of methods and materials directed toward the solution of muscle cytoskeletal and membrane protein structures by x-ray diffraction, electron diffraction, and NMR spectroscopy.

- b. New methods for the purification and reconstitution of muscle membrane proteins.
- c. Development of monoclonal and/or recombinant antibodies to cytoskeletal and membrane proteins exhibiting high specificity and affinity and broad cross-species reactivity.

#### **2. Muscle Fitness and Sports Medicine.**

- a. Improve measurement of muscle strength and balance, including refined instrumentation for biomechanical assessment of normal movement and posture.
- b. Develop quantitative methods of assessing postural perturbations and forces relevant to activities of daily living.
- c. Improve imaging and analytical techniques to measure skeletal muscle properties, (e.g., through MRI Imaging and Spectroscopy).
- d. Imaging techniques which allow simultaneous imaging of muscle morphology and metabolism and blood flow.
- e. Development of novel assays or modifications of currently existing assay of muscle metabolism for use with human biopsy samples.
- f. Develop biosensors to detect changes in pressure, temperature, or physiological parameters associated with muscular activity.
- g. Development of treatments for wound healing and improve general understanding of the natural healing process for muscle.
- h. Develop antioxidant interventions to prevent oxidative damage during muscle use and overuse.
- i. Develop cell culture models for rapid testing of treatments for muscle injury and wasting.

#### **3. Development and Genetic Diseases.**

- a. Develop animal models that mimic the pathophysiology of the genetic human muscle diseases.

- b. Develop gene vectors (viral and non - viral), promoter and enhancer elements and related methodologies that could be used for in vivo and ex vivo gene therapy for muscular diseases.
- c. Develop cell lines and tissue cultures for replacement of muscle that has been damaged or destroyed.
- d. Develop markers for muscle satellite cells and use them to characterize availability for muscle repair.
- e. Develop techniques, equipment, and software to enable improved imaging of muscle development and specialization.

A description of other areas of research under investigation may be found at:

<http://www.niams.nih.gov/rtac/funding/grants/ep4.htm>.

#### **Other Research Topic(s) Within the Mission of the Institute**

For additional information on research topics, contact:

##### Genetics and Clinical Studies

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##### Behavioral and Prevention Research

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##### Osteoarthritis Initiative and Diagnostic Imaging

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## **NATIONAL INSTITUTE OF BIOMEDICAL IMAGING AND BIOENGINEERING (NIBIB)**

The NIBIB supports hypothesis-, design-, technology- or problem-driven research relating to the discovery, design, development, translation and assessment of new knowledge in biomedical imaging and bioengineering. This research may utilize, for example, an organ or disease as a model system for development purposes. Also, several Institutes or Centers may collaborate on research of mutual interest.

For additional information about areas of interest to the NIBIB, please visit our home page at (<http://www.nibib.nih.gov/>). This site includes staff contact information by program area (<http://www.nibib.nih.gov/about/stafflist.html>). It also includes links to program announcements and requests for applications that highlight NIBIB areas of special emphasis (<http://www.nibib.nih.gov/research/investigators.htm>). In some cases, these announcements specifically mention the SBIR and STTR grant mechanisms, in other cases they do not. However, it is clear that small businesses could make contributions to the research objectives described in many of these announcements.

### **Division of Biomedical Imaging**

Research on imaging device development, biomedical imaging technology development, image exploitation, contrast agents, informatics and computer sciences related to imaging, molecular and cellular imaging, bioelectrics/ biomagnetics, organ and whole body imaging, screening for diseases and disorders, and imaging technology assessment. Areas that may be of interest to small businesses include, but are not limited to:

- A. Development of imaging devices for evaluation of all levels of biological material from single-copy (oligonucleotides or proteins) to whole body, particularly development of small animal imaging models.
- B. Development of improved imaging techniques in the areas of spatial and temporal resolution, speed of information acquisition, detectors, and contrast resolution.
  1. Development of new methods for obtaining accurate, 3-dimensional depth dose information for radiography.

2. Development of new display technologies for digital imaging systems and methods for their characterization/assessment.
- C. Development of methods that increase the information obtained from images.
  1. Development of image reconstruction algorithms and image pre-processing methods.
  2. Development of new techniques or application of existing techniques to gain additional data from images.
- D. Application of informatics and computer sciences to imaging.
  1. Development of new and effective strategies for classification and estimation, using synthesis and integration of multimodal imaging and modeling approaches with a priori information.
  2. Integrate information content from diverse imaging methods for diagnostic application.
- E. Development of improved organ and whole body image resolution and data display while maintaining or improving minimization of invasiveness, imaging and processing time, costs, and patient discomfort.
- F. Establishment of novel imaging techniques to pinpoint signifying events that mark disease onset and define its biologic characteristics.
- G. Development of novel telehealth instrumentation or technologies that provide and support health care at a distance and can be applied to a broad spectrum of disorders and diseases.

### **Division of Bioengineering**

Research on biomaterials (biomimetics, bioprocessing, organogenesis, rehabilitation, tissue engineering, implant science, material science, interface science, physics and stress engineering, technology assessment of materials/devices), biosensors/biotransducers (technology development, technology assessment, development of algorithms, telemetry), nanotechnology (nanoscience, biomimetics, drug delivery systems, drug bioavailability, microarray/combinatorial technology, imaging devices, genetic engineering, computer science, technology assessment), bioinformatics (computer science, information science, mathematics, biomechanics, computational modeling and simulation, remote diagnosis and

therapy), and surgery (technique development and technology development). Although not exhaustive, topics of interest for SBIR and STTR applications may include the following:

- A. Development of biomaterials. Development of novel synthetic molecules to mimic structural features of biological systems by incorporation of an understanding of natural systems. Development of biomaterials that incorporate biomechanical design features.
- B. Application of in vivo biomechanics for the continued improvement in the design and application of implants, prostheses, and artificial organs.
- C. Development of fabrication techniques including synthesis or milling techniques, controlled and designed crystallization methods, large-scale methods suitable for manufacturing purposes, controlled particle aggregation, and nanoparticle coating techniques.
- D. Development of biologic components involved in development and organogenesis. Synthesis of components that emulate development and organogenesis.
- E. Development of substrates or scaffolds for tissue growth and differentiation.
- F. Development of material science methods for combinatorial chemistry.
  - 1. Development of paradigms and techniques based on combinatorial approaches for the design, synthesis, characterization, assay, and end-use evaluation of complex, novel molecular entities and interactions.
  - 2. Develop of analysis tools that complement combinatorial approaches, including high throughput screening, chemical analysis, and biological assay.
  - 3. Development of tools for information management and dissemination to cope with the large amount of data generated by combinatorial approaches.
- G. Development of improved implant surfaces and interface processes. Development of techniques that can follow depositions on biomaterial surfaces in vitro and in real time.
- H. Development of improved biosensor technology including the design, fabrication, and characterization of non-fouling sensors to be

used in biomedical research and medicine. Development of algorithms or equations that relate the biosensor transducer measurement to biologically or medically relevant information.

- I. Development of analytical and diagnostic systems, such as scanning probe methods and quantum dot dyes, applicable to the nanoscale.
- J. Development of biomimetic nanostructures.
- K. Development of nano-delivery systems for therapeutic agents that are target-specific, that address transport barriers, and that access the targeted areas in optimal quantities and remain in the area for predictable and adequate lengths of time.
- L. Development of paradigms and techniques based on combinatorial approaches for the design, synthesis, characterization, assay, and end-use evaluation of complex, novel molecular entities and interactions.
- M. Development of new techniques to collect and store quantitative data ranging from the genome to the organism and to elucidate functional dynamics in living cells and tissues with sensitivity down to the level of single molecules.
- N. Development of methods to support the transfer and application of population-based health information in clinical settings.
- O. Development of methods for structuring, managing, and analyzing large, distributed, networked, adaptive databases.
- P. Development of visualization standards for 3-D image acquisition, for visualization parameters to categorize various tissues in 3-D models and for interpreting 3-D images.
- Q. Development of techniques for tracking surgical tools in a stereotactic space.
- R. Development of techniques for the diagnosis and treatment of disease at distant locations.
- S. Development of mechanical or electrical devices to improve surgical outcome.

#### **Other Research Topic(s) Within the Mission of the Institute**

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### NATIONAL CANCER INSTITUTE (NCI)

The NCI is the Federal Government's principal agency established to conduct and support cancer research, training, health information dissemination, and other related programs. As the effector of the National Cancer Program, the NCI supports a comprehensive approach to the problems of cancer through intensive investigation in the cause, diagnosis, prevention, early detection, treatment, rehabilitation from cancer, and the continuing care of cancer patients and families of cancer patients. To rapidly achieve the goal, NCI has developed a plan to: (1) sustain at full measure proven, productive research programs, (2) seize extraordinary scientific opportunities made possible by previous research discoveries, and (3) create and sustain mechanisms that build the capacity to allow the scientific community to apply rapidly evolving discoveries and emerging technologies for the benefit of human health.

Many of the topics below are "open-ended" to encourage submission of innovative SBIR/STTR projects that fit within the mission of NCI. For additional information about areas of interest to NCI, please visit our home page at <http://www.cancer.gov/>. The NCI small business site [http://otir.nci.nih.gov/smallbusiness/small\\_sbir.html](http://otir.nci.nih.gov/smallbusiness/small_sbir.html) may also be of interest.

### Center to Reduce Cancer Health Disparities

Established in March 2001, CRCHD is the cornerstone of the Institute's efforts to reduce the unequal burden of cancer in our society. A central goal of the Center is to translate research discoveries into policies and/or services aimed at reducing cancer-related health disparities in racial,

ethnic, elderly and medically underserved communities.

The Center is interested in the following SBIR/STTR applications:

- A. **Communication.** Training tools to help health professionals deal with issues concerning health literacy and cultural competency.
- B. **Health Care and Epidemiology.** Computer software and hardware for hand-held data input and analysis devices; databases and other tools to study patterns of cancer care in underserved communities.
- C. **New Technology.** Instrumentation to facilitate early detection and screening, including telemedicine and remote medical imaging, and bioengineering technology (including nanotechnology) applied to cancer detection and diagnosis in underserved communities.
- D. **Geographic Information Systems.** Simple, low-cost mapping software to overlay cancer patterns with socioeconomic data, health system infrastructure, healthcare, personal behaviors, ethnicity, risk factors, and consumer profiling among underserved communities.
- E. **Human Genomics.** Tools and technology for health care providers using cancer research developments from genomics, pharmacogenetics and proteonomics for underserved populations.

### Division of Cancer Biology

The Division of Cancer Biology (DCB) plans and directs, coordinates, and evaluates a grant- and contract-supported program of extramural basic and applied research on cancer cell biology and cancer immunology, and cancer etiology, including the effects of biological, chemical and physical agents, in the promotion of cancer; maintains surveillance over developments in its program and assesses the national need for research in cancer biology, immunology and etiology; evaluates mechanisms of biological, chemical and physical carcinogenesis and subsequent tumor growth and progression to metastasis; tests for carcinogenic potential of environmental agents; serves as the focal point for the Federal Government on the synthesis of clinical, epidemiological and experimental data concerning biological agents relating to cancer; and maintains the necessary scientific management capability to foster and guide an effective research program. For

additional information, please visit our home page at <http://www.nci.nih.gov/dcb/dcbhom.htm>.

A. **Biological Carcinogenesis.** The Biological Carcinogenesis Branch (BCB) supports research that seeks to determine the role of microbiological agents as factors or cofactors in the etiology of human and animal cancer. The biological agents of primary interest are DNA viruses, RNA viruses, AIDS and AIDS-associated viruses, although the research may encompass all forms of life including bacteria and other microbial agents associated with cancer and use animal models of cancer and cancer vaccines. A wide range of approaches are supported, including basic biochemistry and molecular biology of oncogenic and suspected oncogenic agents, viral oncogenes and associated tumor suppressor genes, pathogenesis and natural history studies, animal models, and preventive vaccine research. The development of technologies to facilitate studies relating to biological carcinogenesis research is also encouraged. Specific research and technologies supported by BCB in this solicitation include but are not limited to the following:

1. Development of reagents, probes, and methodologies to evaluate the etiologic role of oncogenic viruses and other microbial agents (such as bacteria) in human cancer.
2. Development of novel in vitro culture techniques for oncogenic viruses or other microbial agents associated with or suspected of causing human cancer.
3. Development of sensitive, simplified diagnostic kits or reagents for the detection of oncogenic viruses or other microbial agents.
4. Development and characterization of animal models for studies of the mechanism of cancer induction by viruses or other microbial agents. The animals should faithfully mimic the human diseases associated with the virus or other microbial agent.
5. Development of methods (e.g., new-anti-microbial compounds, new vaccine approaches) to avert the induction of neoplasia in humans and animals by oncogenic viruses or bacteria.

6. Development of other novel technologies, methodologies or instrumentation to determine the role of biological agents, especially viruses, in the etiology of cancer.

B. **Cancer Cell Biology.** The Cancer Cell Biology Branch (CCBB) seeks to understand the biological basis of cancer at the cellular and molecular level. This research utilizes lower eukaryote and animal models, and animal and human tumor cells and tissues to analyze the mechanisms responsible for the growth and progression of cancer. Specific research and technologies supported by CCBB in this solicitation include but are not limited to the following:

1. Development of novel methods to study apoptosis.
2. Development of methods to identify and isolate tissue-specific stem cells.
3. Development of markers associated with specific cellular processes or differentiation.
4. New techniques to transfer functional genes, proteins, antibodies, etc. into intact cells or organisms.
5. Development of new in vitro cancer models that closely parallel in vivo conditions.
6. Improved methods to isolate and preserve human cancer cells appropriate for research.
7. New or improved technologies for efficient microdissection of tumor tissue sections. Among other uses, these approaches would be useful for isolation of DNA from tumor tissues at defined stages of tumor progression.
8. Development of human tumor cDNA library banks to study gene expression in cancer.
9. Development and distribution of genomic resources suitable for genomic manipulation or cytogenetic studies.
10. Establishment of new or improved animal models or non-mammalian models (e.g., flies, worms) as research tools to study human cancers. Among other uses, such models could be used to study the role of cancer genes or for analysis of complex traits.

11. Generation of new inbred genetic animal models that transmit defective or altered cancer-related genes.
12. Development of other novel technologies, methodologies or basic instrumentation to facilitate basic cancer research (research tools).

C. ***Cancer Immunology and Hematology.*** The Cancer Immunology and Hematology Branch (CIHB) supports a broad spectrum of basic research focused on the earliest stages of hematopoiesis and tracing the molecular events that lead to the development of all the functional elements of the immune system and, when errors occur, to the development of leukemias and lymphomas. Most research of interest falls into three major areas. The first is the immune response to tumors to include studies of all of the cells (T, B, NK, antigen-presenting, and other myeloid cells) and secreted molecules (antibodies and cytokines) of the immune system that can recognize and affect tumor growth. Emphasis is placed on the regulatory mechanisms responsible for the failure of immune response to eradicate most tumors under normal conditions, and the development of strategies to circumvent these mechanisms. A second major area of interest examines the biology of hematopoietic malignancies to describe the detailed reasons underlying cell's failure to respond to normal growth controls and to develop novel approaches to prevention or therapy. The third distinct area supported is the basic biology of bone-marrow transplantation, including studies of host cell engraftment, graft-versus-host disease, and the basis of the graft-versus-leukemia effect. Specific research and technologies supported by CIHB in this solicitation include but are not limited to the following:

1. Development of improved or novel monoclonal antibody technologies including improvements of methodologies for fusion, production of novel cells as fusion partners, selection and assay of antibody producing clones, and production of new and improved monoclonal antibodies.
2. Synthesis, structure and function of antibodies capable of reacting with tumor cells, agents that induce tumors, agents used in the treatment of tumors, and agents used in the treatment of tumors.

3. Development of in vivo animal models systems that can be used to study the immune response to tumors and the mechanisms of immunotherapy.
4. Synthesis, structure and function of soluble factors that participate in, activate and/or regulate hematopoietic cell growth and the immune response to tumors, including interferons, other lymphokines and cytokines (interleukins), hematopoietic growth factors, helper factors, suppressor factors and cytotoxic factors.
5. Application of biochemical, molecular biological and immunological techniques for identifying tumor antigens that are good targets for the development of vaccine-type strategies of cancer immunotherapy.
6. Development of techniques to enhance the immune response to tumors, including modification of tumor cells and/or antitumor lymphocytes to facilitate cancer vaccine strategies.
7. Development of improved methodology for manipulating bone marrow inoculum to decrease the incidence of graft-versus-host disease without increasing the risk of graft failure or leukemic relapse.
8. Development of improved methodology for increasing the number of peripheral blood stem cells available for harvest for use in transplantation, including improved methods of identifying and removing residual leukemic cells in the autologous transplant setting.
9. Development of methods to identify and define human minor histocompatibility antigens.
10. Development of novel techniques for antigen identification and protein identification in human tumor cells.
11. Development of novel culture systems to improve the expansion of lymphocytes.
12. Development of combinatorial cell culture research tools to better understand expansion of human hematopoietic stem cells.
13. Development of improved techniques for computational simulation/modeling of biological processes involved in immunologic defenses against tumor cells

such as signal transduction, cell cycle progression, and intracellular translocation.

14. Development of other novel technologies, methodologies or instrumentation to facilitate basic research (research tools) in cancer immunology and hematology.

D. **Chemical and Physical Carcinogenesis.** The Chemical and Physical Carcinogenesis Branch (CPCB) supports basic and applied research concerned with cancers caused or promoted by chemical or physical agents. Carcinogenesis research is supported at the molecular level in areas such as the genetics of cell transformation, mutagenesis, tumor promotion, and DNA damage. Mechanistic studies are encouraged in areas such as metabolism, toxicity and physiological distribution of carcinogens, genetics and regulation of enzymes, biochemical and molecular markers, and organ and cell culture systems and animal models. Also of interest are studies on cancer etiology by environmental chemicals, tobacco consumption and exposure, nutritional hazards, alcohol, asbestos, silica, and man-made fibers. CPCB supports studies on endogenous exposure to steroid hormones and the generation of oxygen radicals during normal metabolism, studies on phytoestrogens and xenoestrogens and their impact on the metabolism of endogenous estrogens are also supported, and work on carcinogenicity/mutagenicity, testing procedures and the development of analytical technologies for use in carcinogenesis research. Specific research and technologies supported by CPCB in this solicitation include but are not limited to the following:

1. Development and validation of methods for food treatment, preparation, or processing that will reduce or eliminate carcinogen/mutagen content.
2. Development of rapid analytical techniques for the qualitative and quantitative detection and screening of xenobiotics, chemical contaminants, and carcinogens/mutagens in human foods and biological and physiological specimens.
3. Development of in vitro and in vivo models for basic studies of carcinogenesis in specific organ systems, such as the pancreas, prostate, ovary, central nervous system, kidney, endometrium, stomach, and upper aerodigestive tract.

4. Development of methods for the production of carcinogens, anticarcinogens, metabolites, biomarkers of exposure, oxidative damage markers, and DNA adducts, both labeled and unlabeled, which are neither currently available commercially nor offered in the NCI Chemical Carcinogen Reference Standard Repository. The production of these compounds, in gram quantities, is desired for sale/distribution to the research community.
5. Development of methods for detection, separation, and quantitation of enantiomeric carcinogens, metabolites, adducts, and biomarkers of carcinogen exposure.
6. Development of monoclonal antibodies that are specific for different carcinogen-nucleoside adducts and demonstration of their usefulness in immunoassays. Of particular interest are antibodies to alpha-beta unsaturated carbonyl compounds (such as acrolein and crotonaldehyde) which can form exocyclic nucleoside adducts with DNA, and immunoassays for carcinogen/protein adducts as potential biomarkers of exposure.
7. Development of immunoassays using monoclonal antibodies that are specific for different polymorphs of Phase I and II carcinogen-metabolizing enzymes and repair enzymes. Included, but not limited to, are antibodies to the cytochrome P450 isozymes, glutathione S-transferases, and N-acetyl transferases.
8. Development of rapid, sensitive, and quantitative assays for the identification and measurement of androgens, estrogens, phytoestrogens, and xenoestrogens in complex biological matrices.
9. Development of rapid analytical techniques for the direct measurement of ligand-protein receptor interactions and determination of binding coefficients.
10. Development of analytical instrumentation for the detection and quantitation of extremely low levels of Tritium (<sup>3</sup>H) or <sup>3</sup>H and Carbon-14 (<sup>14</sup>C) from biological samples. Of particular interest is the development of small-sized, accelerator-

based mass spectrometry equipment capable of measuring down to, or below, contemporary background levels of  $^3\text{H}$  and  $^{14}\text{C}$  that would make this sensitive technique more widely available to research groups. The design and development of technologically improved and miniaturized individual components, including ion source, sample preparation (autosampling apparatus), accelerator, and mass spectrometric detectors, are also solicited.

11. Isolation and development, from natural sources and/or synthesis, of potentially anticarcinogenic flavonoids, isoflavonoids, lignans, Vitamin D analogs, hormonal agonists/ antagonists, bioavailable protease inhibitors, and terpene compounds.
12. Synthesis of selective suicide inhibitors of cytochrome P450 isoforms and selective arachidonic acid pathway inhibitors/enhancers for basic biochemical studies and anticarcinogenic potential.
13. Development of invertebrate animal models (such as *Drosophila*, *C. elegans*, clam, and sea urchin) for the study of environmental chemicals and/or hormonal carcinogenesis.
14. Development of more efficient and reliable methods of preserving valuable animal model gene stocks by innovative in vitro techniques.
15. Development of a defined diet for support and maintenance of aquatic and marine fish models of cancer including but not limited to swordtail, zebrafish, medaka, mummichog, guppy, Fugu, and Damselfish.
16. Development of serum free tissue culture media for aquatic and marine fish models of cancer.

E. **DNA and Chromosome Aberrations.** The DNA and Chromosome Aberrations Branch (DCAB) seeks to study the genome at the DNA and chromosome level, including discovery of genes at sites of chromosome breaks, deletions, and translocations, DNA repair, structure and mechanisms of chromosome alterations, epigenetic changes, radiation- and chemical-induced changes in DNA replication and other alterations, and analytical technologies. Specific research and technologies supported by DCAB in this

solicitation include but are not limited to the following:

1. Development of new, improved technologies for characterization of chromosomal aberrations in cancer.
2. Development of new, improved, or high throughput technologies for whole genome scanning for chromosome aberrations in cancer; spontaneous, chemical or radiation induced.
3. New or improved technologies to increase accuracy of karyotypic analyses of tumor specimens.
4. New or improved methods to mutate genes at specific sites, or to replace genes, in intact cells.
5. Development of new, sensitive methods to assess the methylation status of genes.
6. Development and distribution of genomic resources suitable for genomic manipulation or cytogenetic studies.
7. Technologies for assaying for mammalian genes relevant to repair of damage induced by exposure of mammalian cells to ionizing and non-ionizing radiations, with special emphasis on human cells.
8. Methods/approaches to study the repair of DNA lesions induced by exposure of mammalian cells to ionizing radiations (both high- and low-LET).
9. Development and characterization of human cell lines with specific DNA-repair deficiencies.
10. Development of genetic constructs that utilize radiation-responsive regulatory genes to control the expression of targeted structural genes in mammalian cells.

F. **Mouse Models of Human Cancers Consortium.** The Mouse Models of Human Cancer Consortium is a program based in the Office of the Director, DCB. The Consortium has the important goal of providing mouse cancer model-related resources and infrastructure to the research community, in part through various outreach activities. The outreach requirement generates the need for innovative educational or informational materials that convey the content of Consortium meetings and symposia, or document hands-on workshops in which

models or techniques that are pertinent to mouse modeling are demonstrated. The instructional materials may be CD-ROMs, videotapes, Web-based interactive programs, or other media.

G. **Structural Biology and Molecular**

**Applications.** The Structure Biology and Molecular Applications Branch (SBMAB) focuses on structural and molecular studies to explore the processes of carcinogenesis and tumorigenesis. Areas of interest include structural biology, genomics, proteomics, molecular and cellular imaging, enzymology, bio-related and combinatorial chemistry, and bioinformatics, as they apply to cancer biology. Interests also include modeling and theoretical approaches to cellular and molecular dimensions of cancer biology. Specific research and technologies supported by SBMAB in this solicitation include but are not limited to:

1. Development of new technologies to facilitate the analysis and determination of the molecular structure of macromolecules associated with cancer.
2. Development of new, improved, or high throughput technologies for whole genome scanning for gene identification.
3. Development of systems that will automate the technology of culturing or assaying single cells.
4. New or improved technologies for efficient microdissection of tumor tissue sections and the development of tissue arrays.
5. Improved extraction techniques for tumor specimens for subsequent DNA, RNA, and protein analyses.
6. Rapid methods to isolate intact complexes of regulatory proteins and to separate and identify the proteins.
7. New or improved technologies for the preservation of small amounts of DNA/RNA/protein samples
8. Development of new techniques and vectors for transfer of genes, proteins, and antisense molecules into cells.
9. Generation of software and computer models for the prediction of macromolecular structure and function.
10. Development new methodologies for the generation and automation of tumor cDNA libraries.
11. Development of bioinformatic tools for the study of cancer biology including facilitating genome data, gene "mining," cluster analysis, and data base management.
12. Development of novel gene technology (e.g., microarray, differential display technology) for measurement of differential gene expression levels and functional genomics studies.
13. Development of novel proteomic tools for the analysis of protein expression in cancer biology.
14. Combinatorial library approaches for gene function analysis.
15. Computer-based methodologies to assist in the understanding of signal transduction and cancer biology.
16. Methodologies and techniques for the imaging of macromolecules in vitro and in vivo.
17. Development of in vivo imaging technologies for developmental model organisms.
18. Development of other novel technologies, methodologies or instrumentation to facilitate basic research (research tools) in cancer biology.

- H. **Tumor Biology and Metastasis.** The Tumor Biology and Metastasis Branch (TBMB) supports research focused on the interaction of the tumor with its local environment, the mechanism of tumor cells' acquisition of aggressive malignant behavior leading to invasion or metastasis, and the influence of hormones and growth factors on tumor progression. Special emphasis is given to the development of appropriate animal and cellular models of metastasis. Research interests include studies on: (1) the role of cell adhesion molecules and their receptors, the extracellular matrix, and the basement membrane in development, tissue morphogenesis, wound healing, invasion, and metastasis; (2) the role of cytoskeleton and nuclear matrix in cell proliferation, migration, and invasion; (3) studies on gap junctional communications, cell-cell, and tumor-stroma interactions; (4) role of oncogenes, tumor suppressor genes or

metastasis-specific genes in angiogenesis, matrix degradation, or tumor progression; (5) studies on growth factors and their receptors during tumor invasion, angiogenesis, progression and metastasis; (6) proteases during cancer development and progression; (7) mechanisms of organ-specific metastasis; (8) steroid hormones and their receptors in transformation, tumor growth, and in the development of hormone independence during tumor progression (9) the glycobiology of epithelial cell surfaces and functional consequences of aberrant glycosylation on cell adhesion, tumor progression, and metastasis; and (10) vesicular trafficking and membrane biology during cancer progression. Models used in these studies may include animals, tumor tissues/cells, their components or their products. Specific research and technologies supported by TBMB in this solicitation include but are not limited to:

1. New technical strategies to identify and assess the function of components of the extracellular matrix.
2. Development of new in vitro cancer models to study the pathology and biology of solid tumors and tumor bearing animals.
3. New in vivo models of angiogenesis, cancer progression and metastasis.
4. Development of technologies to identify novel factors that modulate angiogenesis.
5. Identification of genes and/or proteins associated with the process of metastasis.
6. Development of improved techniques for computational simulation/modeling of biological processes involved in malignant transformation, persistence, or invasion, such as signal transduction, cell cycle progression, and intracellular translocation.
7. Development of new assays or methods to evaluate tumor cell invasiveness.
8. Development of new assays or methods to study molecules and pathways involved in cell-to-cell signaling or communication.
9. Development of other novel technologies, methodologies or instrumentation to facilitate basic cancer research (research tools).

## Division of Cancer Control and Population Sciences

The Division of Cancer Control and Population Sciences conducts basic and applied research in the behavioral, social, and population sciences, including epidemiology, biostatistics, and genetics that, independently or in combination with biomedical approaches, reduces cancer risk, incidence, morbidity, and mortality. Laboratory, clinical and population-based research, and health care are translated into cancer prevention, detection, treatment, and rehabilitation activities that cross the life span and the entire process of carcinogenesis, from primary behavioral prevention in youth, to screening, treatment, and survivorship. For additional information, please visit our home page at <http://dccps.nci.nih.gov>.

- A. **Epidemiology and Genetics.** The Epidemiology and Genetics Research Program (EGRP) supports research in epidemiology, biometry, genetic epidemiology, molecular epidemiology, nutritional epidemiology, infectious epidemiology, environmental epidemiology, computing methodology, and multidisciplinary activities related to human cancers. Topics of interest include:
1. Development of software or methods for rapid case ascertainment of cancers.
  2. Development of software for allowing biological specimens for genetic and molecular testing of cancers in epidemiology studies.
  3. Development of web-based data collection tools for cancer epidemiology studies.
  4. Development of applicable bioinformatics for molecular and genetic epidemiology research.
  5. Development of state-of-the-art technology for GIS mapping related to cancer epidemiology studies.
  6. Conversion, validation, and documentation of statistical software packages for use in genetic and general epidemiological analyses on microcomputers.
  7. Methods for the detection of biological markers of human exposure, human susceptibility, or nutritional status for use in epidemiological studies.
  8. Development of software for the guidance of biomedical researchers in the



appropriate use of meta-analytic procedures including prompts for necessary data input, suggestions for the best analytic route to pursue, and examples using published data.

9. Development of banks of standard questions about cancer risk factors; suitably referenced for prior use, validity, reliability, and with appropriate evaluation of index questions. The resource should accommodate either interviewer- or self-administered approaches with flexibility to accommodate requests of varying informational depth.
10. Development of geographical information systems with special visualization techniques for the simultaneous assessment of environmental exposures and health outcomes.
11. Improvements in computer-assisted telephone interviewing technology. Such improvements should permit refinements such as branching, rechecking of previous responses, tallies or summaries of the sum of specific responses for comparison with response to a more general question, and the entry of text as well as codes.
12. Development of online hypertextual tutorials on specific areas of biostatistics and epidemiology with appropriate sample problems using relevant data.
13. Development of an improved indexing system for epidemiologic literature and for data banks listing research in progress.
14. Development of educational interactive software packages on cancer genetics susceptibility for clinical/paramedic personnel as well as patients.
15. Development of user-friendly interactive pedigree analysis software for microcomputers.
16. Development of molecular genetic techniques/methods applicable to large-scale epidemiological studies.
17. Development and maintenance of a repository for unreported data on molecular/genetic polymorphisms.
18. Development of educational intervention software packages for women and

minorities exposed to occupational carcinogens.

B. **Multimedia Technology and Health Communication in Cancer Control.**

A major objective of DCCPS is to plan and conduct extramural, grant-supported programs of cancer prevention and control research in medical and community settings that focus on biomedical and behavioral factors that alter cancer risk. Toward this effort, the Multimedia Technology and Health Communication Program promotes innovative ways of translating cancer research into interventions, programs, systems, networks, or products needed by health care professionals or the public to reduce cancer risks, provide treatment options, or address the needs of cancer survivors.

Grant applicants are required to develop, implement, and test the effectiveness of new or existing models of behavior modification or informational/educational applications using computer applications, advanced telephone technologies, videos, cable and broadcast television, radio, virtual reality, animation, digital imaging, handheld and/or other wireless devices, the Internet or the World-Wide-Web in the following categories:

1. **Behaviors Associated with Cancer Risk.**

- a. Nutrition, Diet and Physical Activity: products or programs to increase the consumption of fruits and vegetables and physical activity.
- b. Smoking and Tobacco Cessation Interventions: products or programs that prevent, or promote smoking cessation among high-risk populations, especially children and young adults.

2. **Cancer Genetics.**

- a. Decision-making programs for families and individuals.
- b. Information products on the psychosocial, ethical, and legal issues associated with cancer genetics.

3. **Diverse Populations.**

- a. Population-sensitive screening, assessment, monitoring, educational or training tools.
- b. Communication approaches to use with persons with specific cancers, i.e.,



- breast (project exception – BSE), head, neck, skin or prostate cancer.
- c. Clinical trials education.
4. *Complementary Medicine Approaches.* Mind/body products that improve the quality of life of persons with cancer or cancer survivors.
5. *Innovative Alternative Teaching Methods.* Cost- and time-effective alternative teaching methods or games that promote the comprehension of cancer prevention and control and healthy behaviors.
6. *Survivorship and Quality of Life Issues.* Development of programs or products that:
- Promote physical and emotional well-being.
  - Address pain, fatigue and depression.
  - Complement or enhance the NCI's Facing Forward series.
  - Teach communication skills to providers on how to speak to patients and their families.
  - Track survivors.
  - Assist children with cancer with the transition from adolescence to adulthood.
  - Involve cancer survivors in clinical trials.
  - Provide systematic screening and follow-up tools for cancer survivors.
  - Provide a resource portal.
  - Provide cultural competence in palliative care.
  - Provide post-treatment of cancer patients via telehealth
- CME courses:
- Training programs in CAM and survivorship.
  - Medical treatments and psychosocial models in survivorship.
  - Use and affects of complementary medicine on survivors.
  - Cervical cancer, CAM, and survivorship.
- Diet, nutrition, CAM and survivorship—authentic products vs. quackery.
  - Prevention of long-term stress.
7. *Systems for Primary Care Professionals and Oncologists.*
- Patient screening, assessment, or management programs with tracking components.
  - Integrated systems to track treatment, management and survivorship activities for cancer patients.
  - Training programs for use by primary care providers and train the trainer programs.
  - Interactive curriculum modules, CME courses, training, or screening/assessment programs for health professionals located in remote areas or where insufficient staff is available.
8. *Systems for the Public.* Cancer education, information, prevention, or screening and assessment programs or products for use by the public.
9. *Clinical Trials.*
- Educate the public, especially diverse populations and the elderly, about participating in clinical trials.
  - Develop mechanisms to encourage and track participation in clinical trials. Projects should complement or enhance NCI's Clinical Trials Education Series: <http://oesi.nci.nih.gov/series/cted/index.html>
10. *Cancer Communication and Interactive Media Technology.* Specific STTR topics for non-profit organizations. See Program Home Page: <http://cancercontrol.cancer.gov/hcirb/sbir/>

### Division of Cancer Treatment and Diagnosis

The Division of Cancer Treatment and Diagnosis funds research into the development of tools, methodologies and therapeutic agents that will better diagnose, assess, cure and effectively treat cancer. We support a spectrum of research projects from preclinical exploratory research and development through clinical trials.

- A. **Cancer Diagnosis.** The Cancer Diagnosis Program (CDP) supports the development of technologies, reagents, instrumentation, and methodologies to improve cancer diagnosis or prognosis or to predict or assess response to therapy. This does not include technologies for imaging of patients. CDP also supports the adaptation or improvement of basic research technologies for use as clinical tools. Technologies supported by CDP may be designed to work with tissues, blood, serum, urine, or other biological fluids. Technologies supported by CDP include but are not limited to the following:
1. Technologies for comprehensive and/or high throughput analysis of molecular alterations at the level of DNA, RNA, or protein. Includes for example, mutation detection systems, gene expression arrays, systems for monitoring epigenetic changes (alternative splicing or methylation), high throughput proteomics (including post-translational modification and protein-protein interactions and methods for protein quantitation).
  2. Micro-electro mechanical systems (MEMs) and other nanotechnologies for the analysis of DNA, RNA, or protein (e.g., micro-capillary systems, lab on a chip applications, micro-separation technologies).
  3. Mass spectrometry for the analysis of nucleic acids or proteins.
  4. Discovery and development of new or improved diagnostic markers or probes targeting changes in DNA, RNA, or proteins, including the generation of molecular diversity libraries by phage display and other combinatorial techniques, and affinity-based screening methods.
  5. cDNA library technologies, including improved methods for generating high quality cDNA clones and libraries and methods for generating high quality cDNA from tissues (including archived specimens).
  6. Resources for clinical research.
    - a. Instruments, technologies or reagents for improved collection, preparation, and storage of human tissue specimens and biological fluids.
  - b. Improved methods for isolation and storage of DNA, RNA, or proteins.
  - c. Tissue and reagent standards: development of standard reagents such as representational DNA, RNA, and proteins and standard tissue preparations to improve the quality of or facilitate the validation of clinical laboratory assays.
  - d. Methodologies for directed micro-sampling of human tissue specimens, including for example, new or improved methodologies for tissue microarrays.
7. Tissue preservation: fixatives and embedding materials or stabilizers that preserves tissue integrity and cellular architecture and simultaneously allows molecular analysis of DNA, RNA, or proteins.
  8. Bioinformatics.
    - a. Methods for acquisition and analysis of data associated with molecular profiling and other comprehensive molecular analysis technologies, including for example, analysis of microarray images and data as well as methods to combine, store and analyze molecular data produced by different techniques (e.g., combined analysis of proteomics and gene expression data).
    - b. Methods for collecting, categorizing or analyzing large data sets containing pathology data or histological images and associated clinical or experimental data, including for example, tumor marker measurements, tissue microarray data, and other relevant biological information.
    - c. Software/algorithms to interpret and analyze clinical and pathology data including methods that relate data from clinical databases to external data sources. Includes for example, neural networks, artificial intelligence, data-mining, data-trend analysis, patient record encryption protocols, and automatic diagnostic coding using standard nomenclatures.
    - d. Informatics tools to support tissue procurement and tissue banking activities.

9. Statistical methods and packages designed for data analysis including correlation of clinical and experimental data.
  10. Automated Cytology.
    - a. High resolution image analysis for use with specimens (e.g., blood, tissues, cells) and tissue microarrays.
    - b. Instrumentation including microscopy and flow cytometry.
    - c. CGH, FISH, immunohistochemical staining and other hybridization assays using probes with fluorescent or other novel tags.
    - d. Methods for single cell isolation and sorting.
    - e. Methods for single cell classification and analysis.
  11. Instrumentation for the detection and diagnosis of tumors, including endoscopy and magnetic resonance spectroscopy (MRS).
  12. Immunoassays using monoclonal, polyclonal, or modified antibodies. Affinity-based binding assays using libraries of aptamers including chemical ligands, small peptides or modified antibodies.
- analogs of complex antitumor structures that retain antitumor activity.
- b. Develop computer modeling and biophysical techniques such as x-ray crystallography and NMR spectroscopy.
  - c. Design prodrugs of anticancer agents that are selectively activated in cancer cells.
  - d. Discover new anticancer agents aimed at relevant targets that exploit unique properties of tumors, that induce or modulate apoptosis, or that induce or modulate differentiation.
  - e. Design and synthesize anticancer prodrugs, latent drugs, or modifiers of cancer drug metabolism or excretion.
  - f. Develop ways to produce adequate quantities of promising natural products or natural product derivatives through total synthesis.
  - g. Develop scale-up technology for the synthesis of materials with promising anticancer potential.
  - h. Develop chemical libraries for anticancer drug screening programs. The generation of small molecular weight libraries (<700 MW, e.g., non-polymeric organic molecules, transition-state analogs, cyclic peptides, peptidomimics) is encouraged.
  - i. Develop array technologies for drug discovery.

For additional information about areas of interest to the CDP Technology Development Branch, visit our home page at: <http://cancerdiagnosis.nci.nih.gov>.

B. **Biochemistry and Pharmacology.** Preclinical studies designed to improve cancer treatment in the following areas: Discovery of new drugs and treatment strategies, selective targeting, development of new preclinical models, pharmaceutical development, and toxicologic evaluations. Emphasis is on molecular targeted approaches. In addition to the topics below, Biochemistry and Pharmacology sponsors special initiatives for Small Business Innovation Research (SBIR) and Small Business Technology Transfer Research (STTR) programs. For additional information, please visit our home page at <http://dtp.nci.nih.gov> and select "Grants/Contracts."

1. **Drug Discovery.**

- a. Design and synthesize novel compounds for evaluation as potential anticancer agents. Synthesize simpler

2. **Drug Evaluation.**

- a. Develop and evaluate anti-metastatic and/or anti-angiogenesis agents or strategies in appropriate model systems.
- b. Develop and evaluate anticancer gene therapy in appropriate model systems. The development of new gene delivery approaches is encouraged.
- c. Develop novel or improved in vitro and in vivo test systems. There is a special need for new types of in vivo tumor models, such as orthotopic tumor models, models using transgenic or knockout animals, models for AIDS-associated malignancies, and models

- to evaluate agents that induce differentiation or apoptosis.
  - d. Develop and evaluate rapid, cost-effective surrogate endpoints to predict clinical efficacy.
  - e. Develop strategies to detect, prevent, or overcome drug resistance.
  - f. Develop novel treatment strategies such as extra corporeal treatment.
  - g. Develop new assays based on molecular targets, especially those that may be amplified or altered in cancer cells. For example, develop assays for agents that interact with oncogenes, suppressor genes, signal transduction pathways, transcription factors, promoters. Assays based on molecular targets that are adapted for high volume screening of chemical libraries are especially encouraged as well as in vivo models, which can be used for "proof of concept" (i.e., validating the selectivity of the agent for the target).
  - h. Develop cost-effective and useful techniques to improve in vitro cell culture methodology, such as the development of automated systems, serum-free media, or carbon dioxide-free buffering systems to stabilize cell culture performance.
  - i. Identify and employ novel targets for antitumor drug discovery utilizing non-mammalian genetically defined organisms, such as fruit flies, worms, zebrafish and yeast.
  - j. Develop technologies such as microarray, proteomics or RNAi, to improve the efficiency of drug discovery.
3. Pharmaceutical Development.
- a. Develop new methods to improve drug solubility for administration of promising antitumor compounds.
  - b. Develop bioavailable alternatives to the intravenous delivery of cytotoxic chemotherapy.
  - c. Develop improved methods to reduce thrombophlebitis and other related side effects observed following intravenous injection of some anticancer drugs.
  - d. Develop new and innovative techniques for sterilization of parenteral dosage forms.
  - e. Develop in vitro and in vivo models to predict human oral bioavailability of anticancer drugs.
  - f. Develop practical delivery systems to deliver anticancer drugs to specific target sites.
4. Toxicology and Pharmacology.
- a. Develop biochemical response profiles of specific target organs (e.g., bone marrow, gastrointestinal tract, liver, kidney, heart, lung) to permit rapid identification of toxic effects resulting from anticancer drug administration.
  - b. Develop in vitro and/or in vivo tests for estimation and prediction of gastrointestinal toxicity, neurotoxicity (central and peripheral), cardiotoxicity, hepatotoxicity, nephrotoxicity and pulmonary toxicity.
  - c. Correlate in vivo and in vitro models for organ toxicity as described above in 4b. Validate for various anticancer drugs.
  - d. Develop drug metabolism (Phase I and Phase II) profiles for anticancer agents in human, mouse, rat and dog liver S-9, microsomes and slices.
  - e. Develop systems to identify toxic effects of drugs by characterizing reactions with biomolecules or receptors.
  - f. Develop in vitro tests to detect, qualify and quantify toxic effects of antineoplastic drugs. Develop techniques for determining individual variations in drug responses due to genetic polymorphisms or other factors.
  - g. Develop a human somatic cell mutagenesis system.
  - h. Develop personal computer programs for pharmacokinetics models capable of predicting drug behavior in humans from preclinical pharmacokinetics data in mice, rats, dogs, and non-human primates.
  - i. Investigate and develop techniques for relating specific enzyme activities (both

- catabolic and anabolic) to body sizes of different species.
- j. Investigate techniques that would allow parameters, e.g., Km and Vmax for enzymes, to be scaled from preclinical to clinical models.
  - k. Develop analytical strategies applicable to the quantitation of potent anticancer drugs in biological fluids at the pg/ml level, e.g., Halichondrin B and Bryostatin.
  - l. Develop non-invasive techniques to determine drug distribution in various animal models.
  - m. Develop gene array technology to determine normal (untreated) and toxicity (cancer drug treated) profiles utilizing samples from various cells and animal tissues.
  - n. Evaluate interspecies transporter distribution and its impact on pharmacokinetic parameters, e.g., the impact of pharmacogenetic variation in biodistribution.
  - o. Determine optimal pharmacokinetic sampling schedules for use in dose titration/pharmacodynamic assessment by integrating information such as pre-clinical pharmacokinetic data, physico-chemical drug properties and mechanism of action.
  - p. Determine which mouse/rat strains provide the most relevant data predict clinical situations (e.g., according to class of compound or mechanism of action).
  - q. Develop an in vitro/in situ system for high throughput drug screens for oral bioavailability.
  - r. Development and delivery of organ specific chemo-protective agents.
5. Animal Production and Genetics.
- a. Investigate alternatives to expensive barrier systems for exclusion of pathogens from rodent colonies, e.g., by use of micro-isolator cages, and evaluate their performance.
  - b. Develop and evaluate specialized shipping containers for pathogen-free animals.
6. Natural Product Discoveries. For the purposes of these topics, examples of natural products in development are: Bryostatin, dolastatin 10, epothilones, and halichondrin B. Note that execution of projects in most of these topic areas will require collaboration and signed agreements with countries where the source organism was originally collected.
- a. Develop techniques for the study of non-culturable organisms in order to identify antitumor agents.
  - b. Develop techniques for the genetic and biochemical characterization and the manipulation of biosynthetic pathways to create leads. Use combinatorial biosynthesis to generate libraries of unnatural natural products as drug leads.
  - c. Use of genetic techniques for the identification of microbial consortia, and for the identification and isolation of genes controlling the biosynthetic pathways producing potential antitumor agents.
  - d. Expression of biosynthetic pathways from microbes or microbial consortia that are known to produce antitumor agents, but in organisms amenable to standard fermentation techniques.
  - e. Investigate new biological methods, such as tissue culture, aquaculture, hydroponics, etc., for the production of natural products as potential anticancer or anti-HIV agents.
  - f. Develop new systems of large-scale production using biotransformation, tissue or cell culture, biotechnology, modification of the chemical ecology of producing organisms, etc., in order to produce the large quantities of anticancer or anti-HIV drugs needed for preclinical or clinical development.
  - g. Develop methods for the isolation, purification, identification, cultivation, and extraction of microorganisms from unusual marine or terrestrial habitats for antitumor and anti-HIV screening. Examples are gliding bacteria,



psychrophilic, barophilic, endophytic, thermophilic, and tropical canopy organisms.

- h. Investigate newer methods of isolation and purification, such as super-critical fluid extraction and chromatography, centrifugal countercurrent chromatography or affinity-based separations, in the isolation and purification of natural products with anticancer or anti-HIV activity.
- i. Develop simple immunoassays that can be used to monitor the levels of natural products of interest in simple extracts of the relevant raw material. These assays should be capable of being developed for use "in the field" and also in developing countries.

7. **Data Management Systems.**

- a. Develop data support systems for chemical library programs.
- b. Develop bioinformatic tools to accelerate the identification, functional understanding and validation of drug targets.
- c. Develop "data mining" strategies such as neural networks.

C. **Cancer and Nutrition.** Research to improve the methodology of nutritional assessment in a cancer population. Innovative approaches to evaluate the contribution of nutritional status to response to cancer treatment.

- 1. Research to improve the methodology of nutritional assessment in a cancer population.
- 2. Develop means to evaluate the contribution of nutritional status to response to cancer treatment.

D. **Clinical Treatment Research.** Clinical research studies designed to improve cancer treatment. Emphasis is on clinical trials for the evaluation of new therapeutic agents, development of assay systems to measure patient response to chemotherapy, development of prognostic assays, and development of methods of analysis and management of clinical trials data.

1. **Evaluation of New Cancer Therapies.**

- a. Conduct clinical trials for the evaluation of new therapeutic agents or modalities of treatment employing drugs, biologics or surgery.
- b. Clinical trials using "unconventional therapies," including, but not limited to, behavioral and psychological approaches, dietary, herbal, pharmacologic and biologic treatments, and immuno-augmentative therapies.
- c. Development and evaluation of new clinical approaches using gene transfer or gene therapy technologies.
- d. Development and evaluation of new clinical approaches using tumor associated antigens or vaccines in order to enhance immunogenicity.
- e. Develop and characterize novel chemical compounds that may be useful anticancer agents, either alone or in combination with other modalities such as radiotherapy.
- f. Develop techniques to lessen the toxicity of existing anticancer treatments.
- g. Develop new techniques for the delivery of anticancer agents that will maximize therapeutic effects and minimize toxicity.
- h. Develop new surgical techniques or tools or improve existing techniques that are/may be utilized in cancer treatment.
- i. Characterize and produce clinical grade monoclonal antibodies to detect and treat malignancies.

2. **Development of Prognostic Assays to Monitor Patient Response to Therapies.**

- a. Develop assay systems to measure the response of human tumors to chemotherapy or biologics.
- b. Characterize drug resistance mechanisms and design methods to overcome clinical drug resistance.
- c. Develop assays for prognostic factors to identify patient subsets who may benefit from specific cancer treatment therapies.

- d. Development of assays to assess effects of agents on specific molecular targets in clinical studies.
- e. Develop new techniques for relating past preclinical information to past clinical results for prediction of future useful clinical agents from future preclinical data (both in vitro and in vivo).

### 3. Clinical Trials Informatics.

- a. Develop new tools and methodologies for the analysis of clinical trials results.
- b. Develop new informatics tools to facilitate clinical trials data entry from the bedside and coordination of data entry and transmission throughout the institution and to other collaborating institutions or organizations.
- c. Development of novel web-based approaches to clinical trials informatics for transmission of data to NCI or other organizations. Topics include point of treatment data capture and reporting, electronic protocols, OLAP (On-line Analytical Processing), support for the Common Toxicity Criteria, and drug accountability support.
- d. Develop new interchange standards, based on technologies such as XML, for sharing data among heterogeneous systems. Specific applications areas include, Adverse Event Reporting, Case Report Forms.
- e. Develop new tools for support of Common Data Elements.
- f. Develop new approaches for interface with electronic medical records, with intent to streamline data reporting, registration, and toxicity reporting of Clinical Trial information.

E. **Biomedical Imaging Program.** The Division of Cancer Treatment and Diagnosis funds research in the development of tools, methodologies and therapeutic agents that will better diagnose, assess, cure and effectively treat cancer. We support a spectrum of research projects from preclinical exploratory research and development through clinical trials.

- 1. Development of medical imaging systems for early cancer detection, screening, and interventions including therapy.
  - a. Development of preclinical and clinical in vivo imaging systems, methods, imaging probes and contrast agents and related image reconstruction, image processing, image display and image-based information as required to detect, classify, monitor and guide delivery to cancer and precancerous conditions.
  - b. Development of methods to assess the value of imaging procedures for the above goals.
  - c. Development of systems, methods and their optimization for studying the adverse reactions of imaging studies.
  - d. Any other investigator-initiated research idea that is relevant to cancer biomedical imaging.

F. **Radiation Research.** The Radiation Research Program (RRP) supports basic, developmental and applied research (including clinical) related to cancer treatment utilizing ionizing and non-ionizing radiations. Therapeutic modalities include photon therapy, particle therapy, photodynamic therapy (PDT), hyperthermia, radioimmunotherapy (RIT) and boron neutron capture therapy (BNCT). Radiation research encompasses a range of scientific disciplines including basic biology, chemistry, physics and clinical radiation oncology. Topics of interest include, but are not limited to, the following areas:

- 1. Development of devices for planning and delivering radiation therapy or related therapies, including devices for patient positioning and quality assurance for the following: (a) ionizing radiation, particularly 3-dimensional conformal radiotherapy (3DCRT) and intensity-modulated radiotherapy (IMRT); (b) PDT; (c) hyperthermia; and (d) RIT.
- 2. Development of devices for dosimetry for (a) ionizing radiation; (b) PDT, particularly those capable of measuring light doses at depth in tissues; (c) thermometry for hyperthermia, particularly non-invasive thermometry; and (d) RIT.

Devices may include chemical, solid state, film, biological or ionization systems to detect or read out exposures. Accuracy, precision and linear response are essential over the range of doses and temperatures employed in the research laboratory and/or in the clinic, depending on their intended use. Devices for thermometry during hyperthermia treatment must give accurate readings with the heating device(s) with which they are to be used.

3. Development and evaluation of computer hardware and software for radiation therapy, such as computation algorithms, computer workstations, image guidance techniques, and informatics methods for treatment planning, delivery and outcomes analysis.
4. Development of novel drugs to increase the effectiveness of radiation therapy or related therapies: (a) chemical modifiers of radiation response, particularly small molecules directed at molecular targets involved in tumor radioresistance; (b) photosensitizers for PDT; (c) sensitizers for use with hyperthermia; and (d) prodrugs that are selectively activated within the tumor.
5. Development of drugs to prevent, reduce or reverse normal tissue response, especially the late effects that develop months or years after therapy.

Compounds that are based on a rationale for achieving a therapeutic gain (an improved differential response between tumor and normal tissue) are of greatest interest. Enhancement of response must be achieved at radiation doses and treatment schedules employed clinically.

6. Development of predictive assays and monitors of response to radiotherapy, PDT, hyperthermia or RIT. Tools are needed to identify patients that would benefit from specific therapeutic approaches.

G. **Biological Response Modifiers (BRM).**

Research on agents or approaches that alter the relationship between tumor and host by modifying the host's biological response to tumor cells with resultant therapeutic benefits. Both preclinical and clinical investigations are conducted on the utility of a wide variety of natural and synthetic agents and on biological

manipulations of immunological and non-immunological host mediated, tumor-growth controlling mechanisms in cancer therapy.

In addition, development of new approaches to modify host responses to the human immunodeficiency virus (HIV) is included in the scope of this announcement.

Studies are encouraged which utilize in vitro assays and/or animal model systems to investigate mechanisms of BRMs. Examples of innovative research that would be responsive to this solicitation include:

1. Application of observations describing shared receptors and mediators between the neuroendocrine and immune systems in studying immunobiology and immunotherapy of cancer or AIDS.
2. Evaluation of molecular genetic approaches to discovery of new therapeutic agents, delivery of BRMs, or development of gene therapy.
3. Studies of new agents active in inhibiting the development and/or reversing, multidrug resistance at the genetic and immunological level.
4. Development of improved techniques to synthesize, screen and develop new oligonucleotides for anti-oncogene or anti-viral effects.
5. Improvement in cell-culturing techniques, e.g., by developing automated cell culture systems, specialized media, or improved methods to induce activation, proliferation or differentiation.
6. Determination of new antitumor therapeutic approaches with maturation, differentiation or growth properties.
7. Development of new procedures or reagents for the modulation of the suppressor arm of the immune system in experimental models, directed towards successful immunotherapy.
8. Improvement of tumor-associated antigens or vaccines in an attempt to enhance immunogenicity.
9. Development of novel in vitro assays for the primary screening of BRMs.

## Division of Cancer Prevention

The Division of Cancer Prevention (DCP) directs an extramural program of cancer prevention research including chemoprevention, nutritional science, genetic, epigenetic, and infectious agent, early detection including biomarker development and validation and biometry for the Institute. DCP also supports research training and career development in cancer prevention and early detection and coordinates community-based clinical research in cancer prevention and dissemination of cancer treatment practice through a consortium of community clinical centers. For additional information, please visit our home page at <http://dcp.nci.nih.gov/>.

- A. **Prevention.** Research studies to identify, evaluate, and implement techniques and approaches for the prevention, risk assessment, and early detection of cancer. Those studies capable of achieving these objectives with minimal risk and cost are preferred.
1. **Chemoprevention.** Studies in which naturally occurring or synthetic agents are identified, or further evaluated for efficacy or safety. Studies involving in vitro assays with cell transformation systems, in vivo assays involving animals models to evaluate agents against typical carcinogenic agents at specific sites, and studies involving clinical chemistry measurement of agents in sera or other biological fluids are of highest program relevance. Studies aimed at improving future research designs for chemopreventive trials; providing additional biological understanding, identification and evaluation of modulation of quantitative or qualitative biological endpoints, and/or markers for surveillance of compliance will also be considered. Examples of tests might include measurements of biochemical parameters, cytological screening techniques, in vitro studies of suppression of oncogene protein products, enhancement of tumor suppressor genes, in vitro toxicological studies, and synthesis of novel chemopreventive agents based on structure/activity relationships.
  2. **Diet and Nutrition.** Studies that aim to reduce the incidence of cancer through dietary modification, which may include additions, deletions, or substitutions of

foods or dietary factors. Studies aimed at dietary assessment and measures of compliance to the dietary modification are relevant to these dietary modification studies. Studies that can provide further understanding of the relationship between dietary components and cancer risk and the influence of dietary changes on biochemical indices, hormonal milieu and immune function will also be considered.

- B. **Community Oncology.** Introduction, application, and evaluation of effective and practical cancer control intervention programs in community settings. Primary emphasis is on the integration and involvement of community physicians and allied health professionals in cancer control efforts and the promotion of linkages between community practitioners/hospitals and other regional resources for cancer control.

Objectives are to: (1) reduce the time between research advances in prevention, detection, and patient management and their application in community settings; and (2) expand extend the cancer care knowledge and applications bases; and (3) evaluate new detection and diagnostic methods for specificity, sensitivity, reliability, validity, safety, feasibility and cost when applied to defined or target populations. This may include screening research as well.

- C. **Rehabilitation and Continuing Care.** Development and evaluation of rehabilitation or continuing care strategies which directly enhance functioning of patients with cancer or which contribute to understanding of factors impacting utilization of supportive services by cancer patients. Clinical applications include development and testing of interventions to enhance multidisciplinary approaches to cancer rehabilitation, and research on effective symptom management (e.g., cancer-related pain, fatigue, nausea, mucositis). Areas of general program interest include innovative approaches to measuring and enhancing quality of life of cancer patients; research to investigate and enhance clinical decision-making by both patients and physicians; and studies of the impact of individual preferences for health care outcomes and their impact on cancer prevention practices in persons without cancer and on treatment decisions in patients with cancer.

- D. **Early Detection and Screening.** New diagnostic or screening methods for early detection of cancer, especially for asymptomatic patients. Detection methods can include any cancer site, although there is more interest in the common cancers, such as those of the lung and colon. Methods should be cost beneficial and applicable in a clinical setting.
1. Studies which identify and document new databases relevant to early cancer detection and propose using new and experimental analytical techniques.
  2. Analyses of long-term, follow-up data from completed studies for potential new interpretations based on the passage of time.
  3. Studies which propose to develop and evaluate new detection techniques and measures for sensitivity specificity, reliability, validity and safety.
  4. Determinations of the cost/benefit or risk/benefit ratios of cancer screening and detection methods when applied in defined or target populations.
  5. Currently, the most commonly used method to detect prostatic cancer is the digital rectal examination. Various devices and models would be necessary for the early detection of prostate cancers by physical examination. They would include, but not limited to the following disease states: (1) absence of disease (normal model); (2) benign prostatic hypertrophy; (3) prostatitis; (4) Stage B1 prostatic cancer (T2a); (5) Stage B2 prostatic cancer (T2b); and (6) Stage C prostatic cancer (T3z, T3b, and T4).
  6. Development of products that aid the systematic collection and transport of specimens used for the early detection of cancer, including devices for the collection and transport of urine, serum, fecal material, exfoliated cells, and other potential materials.
  7. Develop computer utility programs that can increase the clinical uses of existing programs commonly found in medical offices creating age-sex registries, predicting population risks, determining screening needs of patients, reminder systems, etc. Develop bioinformatics to study gene profiling.
  8. Develop personal computer programs that can be used to determine population risks and the effect of interventions. These programs might also be adopted to the concept of Community Oriented Primary Care.
  9. Use of ultrasonography with color flow imaging for the early detection of cancer. Research on the use of ultrasonography with color flow imaging (US-CFI) for the early detection of cancer of the ovary, breast and/or prostate. Emphasis should be given to the ability of the US-CFI to differentiate between malignant and benign disease at these sites. Criteria for the discrimination of malignant from benign disease would be developed as well as performance characteristics of this method, particularly for breast and prostate. Studies on symptomatic populations should yield sensitivity, specificity and positive predictive values when breast and prostate are the target sites. Studies on asymptomatic populations should yield sensitivity, specificity and positive predictive values when ovarian cancer is the target site.
  10. As more women seek mammographic breast screening, the importance of efficient, high speed, "intelligent" mammographic systems capable of acquiring and storing large volumes of images and enhancing image interpretation will become more important. Technological developments of interest are:
    - a. Develop digital mammographic systems for high volume applications with electronic archiving and image analysis capabilities.
    - b. Develop artificial intelligence based interactive image analysis software to enhance mammographic sensitivity and specificity.
- Other Research Topic(s) Within the Mission of the Institute**
- For additional information on research topics, contact:
- Ms. Connie Dresser  
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(301) 435-2846, Fax: (301) 480-2087  
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Websites: <http://cancer.gov/>  
[http://otir.nci.nih.gov/smallbusiness/  
small\\_sbir.html](http://otir.nci.nih.gov/smallbusiness/small_sbir.html)

#### **CENTER TO REDUCE CANCER HEALTH DISPARITIES**

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#### **DIVISION OF CANCER BIOLOGY**

[HTTP://DCB.NCI.NIH.GOV](http://DCB.NCI.NIH.GOV)

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#### **DIVISION OF CANCER CONTROL AND POPULATION SCIENCES**

[HTTP://DCCPS.NCI.NIH.GOV/](http://DCCPS.NCI.NIH.GOV/)

*Cancer Epidemiology and Genetics*  
<http://epi.grants.cancer.gov/>

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*Multimedia Technology and Health Communication  
in Cancer Control*

<http://cancercontrol.cancer.gov/hcirb/sbir/>

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#### **DIVISION OF CANCER TREATMENT AND DIAGNOSIS**

[HTTP://WWW3.CANCER.GOV/DCTD/](http://WWW3.CANCER.GOV/DCTD/)

*Cancer Diagnosis Program*  
<http://www.cancerdiagnosis.nci.nih.gov/>

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*Biochemistry and Pharmacology*

<http://dtp.nci.nih.gov>

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*Cancer Therapy Evaluation Program*

<http://ctep.cancer.gov/>

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*Biomedical Imaging Program*

<http://www3.cancer.gov/dip/>

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*Radiation Research Program*

<http://www3.cancer.gov/rpr/>

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*Biological Response Modifiers*

<http://web.ncifcrf.gov/>

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**DIVISION OF CANCER PREVENTION**

[HTTP://WWW.CANCER.GOV/PREVENTION/](http://www.cancer.gov/prevention/)

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For NCI-related SBIR Information, visit:  
<http://www3.cancer.gov/admin/gab/index.htm>

**NATIONAL INSTITUTE OF CHILD HEALTH AND HUMAN DEVELOPMENT (NICHD)**

The NICHD conducts and supports research and research training on biological and behavioral aspects of human development. Primary program areas include: reproduction and population studies, pregnancy, perinatal biology, maternal and infant well-being, developmental and reproductive immunology, congenital defects, developmental biology, teratology, nutrition and growth, human learning and behavior, learning disabilities, cognitive and social development, mental retardation and developmental disabilities, pediatric, adolescent, and maternal AIDS and HIV, obstetric and pediatric pharmacology, and medical rehabilitation.

For additional information about areas of interest to the NICHD, please visit our home page at <http://www.nichd.nih.gov>.

**Population Research**

Research on topics in reproductive sciences, contraceptive development, and demographic and behavioral sciences. Examples of research topics that may be of interest to small businesses include, but are not limited to:

- A. **Reproductive Sciences.** Research on the reproductive processes of men and women and of animals with similar reproductive systems

related to developing safer and more effective means of regulating, preserving or achieving fertility. Particular areas of programmatic interest relative to small business initiatives include, but are not limited to:

1. Development of reagents to facilitate study of reproductive and developmental processes.
2. Establishment and validation of functional cell lines.
3. Development of novel assays, kits, and devices to monitor fertility.
4. Development of high resolution technologies to provide invasive or noninvasive assessments of reproductive and developmental competence.
5. Development of experimental animal models that would be useful for studying the physiology and pathophysiology of reproductive processes.

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- B. **Contraception and Reproductive Health Research.** Emphasis is on developing new and improved methods of fertility regulation; developing new and improved treatments for disorders of the reproductive system including female pelvic floor disorders; and research on the benefits and risks of contraceptives and other drugs, devices, and surgical procedures as they affect reproductive health. Areas of interest include, but are not limited to:
1. Developing new and improved methods of fertility regulation, for men and for women that are safe, effective, inexpensive, reversible, and acceptable. This includes, but is not limited to, synthesis and testing of novel chemical compounds.
  2. Developing new and improved treatments for disorders of the male and female reproductive system, including those used for hormone therapy and drugs, graft materials, and devices used for non-surgical and surgical treatment of pelvic organ prolapse, urinary incontinence, and other female pelvic floor disorders.
  3. Discovering and disseminating new knowledge about the medical benefits and risks of contraceptives and other drugs,

devices, and surgical procedures affecting reproductive health. We will primarily support applied research projects such as epidemiologic studies or Phase III/IV trials designed to detect clinically significant adverse effects, particularly those too rare to be determined through the FDA's premarketing approval process. Laboratory models will be used when human studies are not feasible or to explore mechanisms of action or supplement epidemiologic and clinical observations.

4. Studies relating contraception or reproductive health to STDs such as HIV, including but not limited to development of new products with microbicidal activity against STDs such as HIV; studies to define the relationships among contraceptive methods and HIV acquisition, transmission, or disease progression; development of diagnostic and other research models for HIV and contraception/reproductive science; and studies to clarify mechanism of interaction between contraceptives and other disease processes or conditions.

Dr. Steven Kaufman  
(301) 435-6989, Fax: (301) 480-1972  
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C. **Demographic and Behavioral Sciences.**

Research on the size, growth, and composition of populations and the impact of changes in population on the health and well-being of individuals, families, and the population itself. The program emphasizes not only factors affecting fertility, mortality, population movement and compositional change, but also teenage childbearing, AIDS, single-parent families, racial and ethnic differentials in infant mortality, legal and undocumented immigration, and the well-being of children. Applications are encouraged in these areas:

1. Innovative use of geographical information systems and spatial network analysis.
2. Innovative approaches to analyzing and disseminating large-scale data sets.
3. Development of effective tools for prevention research and intervention programs related to STD/HIV, pregnancy, divorce, child health, and other mission-related topics.

4. Innovative approaches to teaching population studies and other behavioral and social sciences at the undergraduate and graduate level.

Dr. Rebecca Clark  
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**Research for Mothers and Children**

Research in eight major program areas includes: pregnancy and perinatology; developmental biology, genetics and teratology; endocrinology, nutrition, and growth; mental retardation and developmental disabilities; learning disabilities; cognitive and social development; obstetric and pediatric pharmacology, and pediatric, adolescent, and maternal AIDS. Topics that may be of interest to small businesses include, but are not limited to, those identified below.

- A. **Pregnancy and Perinatology.** Research on the physiology of pregnancy and labor; high-risk pregnancies, including those with hypertensive disorders, diabetes or seizure disorders; fetal pathophysiology; premature labor and birth; disorders of the newborn; sudden infant death syndrome; and biological and behavioral antecedents of low birth weight.

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- B. **Developmental Biology, Genetics, and Teratology.** Biomedical research on the cellular, molecular, and genetic aspects of normal and abnormal embryonic and fetal development and its aberrations, including early embryogenesis, limb formation, development of the nervous system, developmental and reproductive immunology, and causative factors in teratogenesis. Applications to develop and apply new animal model systems or innovative and high throughput genomic and proteomic technologies to advance the study of embryonic development, structural birth defects, and newborn screening are particularly welcome.

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- C. **Endocrinology, Nutrition, and Growth.** Research on the nutritional needs of pregnant women and their fetuses; aspects of nutrients

related to reproduction, growth, and development; breast feeding and lactation; the immunology of breast milk; development of the gastrointestinal system; childhood obesity and the nutritional antecedents of adult disease; developmental endocrinology; mechanisms of hormone action during growth and development, and the impact of hormonally active agents in the environment on growth and development. Applications to advance the study of obstetric and pediatric pharmacology include: Research and tools to better characterize the impact of physiological and developmental changes on pharmacokinetics and pharmacodynamics; advancements in modeling which improve therapy during pregnancy, among premature infants, children and adolescents; research on tools to monitor the state of various organ systems during therapy in pregnancy or infancy; such as, cerebral monitors, placental function, etc.; models to characterize molecular, dosing or other modification to improve therapy.

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- D. **Mental Retardation and Developmental Disabilities.** Biomedical research in neuroscience, genetics, biochemistry, molecular biology, and psychobiology aimed at identifying factors that cause abnormal brain maturation and function; identification of direct and indirect social, economic and cultural influences on the occurrence of mental retardation and developmental disabilities (MRDD); and research leading to the assessment, prevention, and amelioration of MRDD, including screening and prenatal diagnosis.

Dr. Mary Lou Oster-Granite  
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- E. **Child Development and Behavior.** Research and research training programs in developmental psychology (cognitive, affective, and social development), cognitive psychology, cognitive neuroscience, language acquisition and bilingualism, developmental neuropsychology, and educational psychology; studies to define, classify, and map the developmental course of specific learning disabilities and disorders of attention; studies to elucidate the etiological role of cognitive,

linguistic, perceptual, educational, genetic, social, and neurobiological mechanisms in dyslexia, learning disabilities, language disorders, and disorders of attention; investigations of the effects of well-defined treatment interventions on specific types of learning disabilities; studies designed to understand the development of attention, reasoning, planning, problem solving, and concept formation in children; studies delineating the effects of motivation, emotion, societal, cultural, familial, and neurobiological influences on social, emotional, and cognitive development; examinations of the effects of parental and non-parental care on social, emotional, and cognitive developmental outcomes; and investigations of temperament, motivation, self-concept, attitudes, and values, and their relationship to development. Research and development of neuroimaging tools specific to brain development in pediatric populations and including research or tool development using EEG, magnetic resonance imaging (MRI), functional MRI, magnetic spectroscopy, and near infrared spectroscopy.

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- F. **Pediatric, Adolescent, and Maternal AIDS.** Research on all aspects of HIV (human immunodeficiency virus) infection and disease, including AIDS in women of child-bearing age, pregnant women, mothers, fetuses, infants, children, and adolescents. Areas of interest include, but are not limited to, epidemiology, natural history, pathogenesis, treatment, and prevention.

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### Medical Rehabilitation Research

Research is encouraged on the restoration, replacement, or enhancement of functioning required by children or adults with physical disabilities to be effective in daily life. The mission of the NCMRR is to increase the effectiveness of medical rehabilitation practices through research on:

- A. Improving functional mobility.
- B. Promoting behavioral adaptation to functional losses.

- C. Assessing the efficacy and outcomes of medical rehabilitation therapies and practices.
- D. Developing improved assistive technology.
- E. Understanding whole body system responses to physical impairments and functional changes.
- F. Developing more precise methods to measure impairments, disabilities, and societal limitations.
- G. Training health professionals in the field of medical rehabilitation.

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#### Other Research Topic(s) Within the Mission of the Institute

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#### NATIONAL INSTITUTE ON DRUG ABUSE (NIDA)

The mission of the NIDA is to lead the nation in bringing the power of science to bear on drug abuse and addiction, through support and conduct of research across a broad range of disciplines and by ensuring rapid and effective dissemination and use of research results to improve prevention, treatment, and policy. For additional information about areas of interest to the NIDA, please visit our home page at <http://www.nida.nih.gov/>.

#### Division of Treatment Research and Development

The NIDA DTR&D supports research aimed at the development and testing of pharmacological and behavioral treatments for drug abuse and addiction. This includes the identification, evaluation, development, approvability, and efficacy testing of new and improved pharmacotherapeutic agents, as well as the testing of marketed medications, and of behavioral treatments used alone or integrated with medications. The DTR&D also advances a human neuroscience research and training program focused on understanding the neurobiological substrates of drug abuse and addiction processes.

- A. **Chemistry and Pharmaceuticals Branch (CPB)**. The CPB supports research in the design (including molecular modeling and structure-activity relationship studies) and synthesis of novel compounds, formulation development, bioanalytical methods development, and pharmacokinetics/pharmacodynamics aimed at the discovery and development of new medications for treating drug addiction. (NIDA-CPB). Areas that may be of interest to small businesses include, but are not limited to research related to the design and development of new compounds and improved drug products (drug delivery) for the treatment of drug addiction:

1. Synthesis of new chemical compounds that would have potential as treatment agents for the medical management of stimulant (e.g., cocaine, methamphetamine, or nicotine) addiction. Consideration should be given to the design of partial agonists or pure antagonists that diminish the reinforcing effects of stimulants, as well as full agonists that could function to normalize physiological activity following discontinuation of stimulant use.

Compounds of interest include those that are designed to affect dopaminergic (i.e., D1 agonists, D3 agonists and D3 antagonists) activity, CRF antagonists, compounds affecting glutamate activity, GABAergic activity, small molecule neuropeptide antagonists and compounds acting through other mechanisms for which justification has been supplied.

2. The development of combinatorial libraries for discovery of drug addiction pharmacotherapies.



3. Synthesis of new chemical compounds with potential for the treatment of opioid dependence and/or craving. Compounds which may prevent relapse to opiate use following a period of drug abstinence are of special interest. Kappa antagonists are of particular interest.

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4. Development of new approaches for the administration of potential addiction treatment drugs with poor bioavailability.
5. Development of controlled release dosage forms for addiction treatment medications in order to maintain therapeutic drug levels for extended periods of time to alleviate compliance problems associated with addiction treatment.

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- B. Medications Discovery and Toxicology Branch (MDTB).** The MDTB supports research on the development of preclinical behavioral models (e.g., of craving, drug-seeking behavior, dependence, or relapse), biochemical assays, gene expression assays and electrophysiological methods to identify and characterize new medications to treat substance abuse, as well as pharmacological screening of novel compounds to identify potential drug abuse medications. The Branch also supports research on toxicity studies of potential medications for the treatment of substance abuse, and interactions of potential treatment medications with abused substances. Areas that may be of interest to small businesses include, but are not limited to development of new methods for discovery of medications useful in treating drug addiction. Of special interest would be the development of new animal models of addiction, incorporating established drug self-administration techniques that show increased relevance to the clinical setting. Development of relevant biochemical or electrophysiological screening methods is also encouraged.

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- C. Behavioral Treatment Development Branch (BTDB).** The BTDB supports research on behavioral treatments and combined behavioral and pharmacological treatments for drug abuse and dependence. Behavioral treatments include psychotherapies, behavior therapies, family therapies, group therapies, counseling strategies, rehabilitative techniques, brief behavioral interventions, therapeutic community treatments, and other psychosocial treatments. Research on these treatments may be carried out in any setting, including both academic and community or "real-world" settings. Areas that may be of interest to small businesses include, but are not limited to:

1. Behavioral Strategies for Increasing Compliance in Taking Treatment Medication. Research to develop and to evaluate strategies to induce recovering addicts to take medication for a prolonged time, especially antagonists such as Naltrexone; to induce HIV infected drug users to comply with medical treatments (HAART) in drug abuse treatment settings; or to adapt existing behavioral strategies to increase patient compliance and cooperation in long-term treatment for drug abuse or for diseases associated with drug abuse such as tuberculosis or hepatitis. An important consideration should be cost and practicality of use in actual clinical practice or in an aftercare program. The product of such research might be a manual, which describes the behavioral strategy, and its implementation by treatment staff or scientific data regarding evaluation.
2. Integration of Behavioral Therapies and Pharmacotherapies. Development and testing of integrated therapeutic approaches for individuals who abuse various drugs, including methamphetamine, cocaine, nicotine, and opioids; in addition this may include individuals with co-occurring substance abuse and mental disorders, since effective treatment of both disorders may lead to improved treatment outcomes. Integrated behavioral therapies and pharmacotherapies may enhance the efficacy of both types of therapeutic interventions. For instance, the maintenance and detoxification of heroin addicts could perhaps be optimized by the integration of distinctive behavioral therapies devised specifically for opioid



agonists, antagonists or partial agonists determined by the heterogeneity of the subgroup of addicts and the pharmacological differences of the medications. Integration of medications and behavioral therapies could possibly enhance compliance with medication regimens, *increase* retention allowing pharmacological effects to occur and prevent relapse to drug abuse and addiction.

3. *Behavioral Treatment Research for Drug Abuse and Addiction in Primary Care.*

Recent research has shown that physicians and other clinicians often fail to recognize drug abuse or addiction among their primary care patients. In addition, a significant number of these clinicians reported that they did not know how to intervene with their patients if drug abuse or addiction was suspected. Drug abuse related illnesses and morbidity often occur in adults and may have begun in adolescence. However, very little research has been done to develop or test behavioral treatment approaches or combined pharmacological and behavioral treatments for drug abuse and addiction in primary care settings. The objectives of this initiative are to encourage research on the development and testing of innovative brief behavioral treatment approaches, alone or in combination with pharmacological treatments that may be used in various primary care patient populations and primary care settings. Other goals of this research initiative are to encourage additional research on the development and evaluation of culturally sensitive screening and assessment instruments for use in primary care; and to encourage research on the transportability of efficacious behavioral treatments to primary care settings, as well as research on science-based training approaches for changing primary care clinicians' behaviors regarding their recognition and intervention with drug abusing or addicted patients. While motivational enhancement approaches for some drug abusing populations have been found to be effective, this behavioral approach has not been widely used in primary care.

4. *Woman and Gender Differences in the Provision of Behavioral Treatments, and HIV/AIDS Risk Reduction Approaches.*

Develop and evaluate specific behavioral treatment approaches targeting drug-addicted women. This may include behavioral therapies, skills training techniques, counseling strategies, and HIV and other infectious disease behavioral risk reduction strategies. This may also include development and testing of training materials that specifically address women and gender differences in drug addiction treatment to promote effective use of research-based treatment approaches. Training materials may involve treatment manuals, training videos, CD ROM or DVD technologies, Internet or computer based programs to manage aspects of treatment administration, or other innovative educational strategies for health professionals using new technologies.

5. *Transporting Behavioral Treatments to Community Practitioners.*

There is a need for effective methods of transferring behavioral therapies found to be effective in clinical trials to clinical practice. Cognitive-behavioral therapy, operant behavioral therapy, group therapy, and family therapy are among the therapies that have been shown to be efficacious in a highly controlled setting and may be helpful treatment approaches in community treatment programs as well. However, community practitioners may have been trained using other approaches and may not have been exposed to these scientifically-based approaches. This is a call for proposals that examine mechanisms to transfer effective research-based drug abuse treatment information and skills-based techniques to practitioners in the community. This may involve the development and testing of innovative training materials and procedures to use in the training of community practitioners to skillfully administer these treatments, including the development of highly innovative technology transfer and communication approaches. Research testing the transportability of empirically supported therapies to the community is an important component of the Behavioral Therapies Development Program.

There is also a need for the development of educational methods to train non-drug abuse health care workers in relating to drug abusers; eliciting medical histories regarding past or present drug abuse; recognition of the signs and symptoms of drug abuse; identification of those at high-risk for HIV and other drug abuse related medical problems such as tuberculosis or hepatitis. Development and validation of a drug abuse screening instrument which can be administered by primary health care providers, and training in administering such an instrument.

6. Using Telemedicine to Disseminate Drug Addiction Research Findings to Primary Health Care Providers. Telemedicine programs are being used in urban medical centers to rapidly disseminate science-based information on new medical treatments. In addition, approximately one-third of the rural hospitals are now using telemedicine to improve patient care. Health care professionals need science-based information on drug abuse prevention and treatment. Research to develop and evaluate telemedicine programs to transport science-based information on drug addiction to the primary health care community is encouraged.
7. Developing, Evaluating, and Transporting Culturally Sensitive Behavioral Therapies for Racial and Ethnic Minorities. Minority populations are disproportionately affected by the consequences of drug abuse. Research to develop and evaluate behavioral treatments that are culturally sensitive and relevant for diverse racial and ethnic minority populations is encouraged. This may include studies of behavioral treatments, alone or in combination with pharmacological treatment, or studies of behavioral strategies for increasing adherence to taking medications. In the development and evaluation of the behavioral treatment, attention needs to be directed at examining medical, social, and cultural factors that may influence adherence to the behavioral treatment approach and treatment outcome. Also, little is known about the transportability of efficacious behavioral treatments for minority populations. Research is needed on how to transport science-based

treatments to various racial/ethnic populations.

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8. Behavioral Therapy Development. Development of new or refinement of existing psychotherapies, behavioral therapies, skills training techniques or drug counseling strategies for the treatment of drug abusers/addicts. Incorporation of HIV risk reduction strategies as an integral component in routine counseling or other behavioral interventions. This would include the development of: therapy manuals, to define exactly what the therapy is and how to administer it optimally; competence and adherence scales, to evaluate the extent to which therapists and counselors are actually providing the therapy intended; process measures, to measure various aspects of the therapeutic interaction; and measures of the integrity and fidelity of the therapy. The following are of particular interest:
  - a. Development of behavioral therapies or components of such therapies that are based on developments and findings from the basic behavioral or cognitive sciences.
  - b. Discrete therapy components that address specific problems common among drug addicted individuals and that can be implemented in conjunction with other therapeutic services. For example, an investigator may wish to develop a four session, highly focused, job seeking skills module that can be easily implemented by a wide range of practitioners to effectively increase appropriate job seeking behavior. Other examples include, but are not limited to, modules to engage ambivalent drug dependent individuals in treatment, modules to increase assertiveness in female drug addicts who feel pressured by others to use drugs, or to incorporate effective HIV risk reduction techniques.
  - c. Therapies designed specifically to engage and retain individuals in treatment, especially those at high risk

for HIV. An example could be a therapy that is: (1) sensitive to the motivational level of the client; (2) is specifically designed to respond to the needs of the individual, whatever his or her motivational level might be; and (3) actively works to increase an individual's desire to remain in treatment.

- d. Therapies designed to intervene with understudied populations including users of drugs such as MDMA and other club drugs, marijuana, and inhalants, as well as personality disordered drug abusers.
- e. Therapies for drug abusers who are not yet dependent on drugs to reduce risk of escalation to dependence and therapies for drug abusers who have not considered or claim little interest in seeking treatment for their drug problems. For these populations treatments are needed which interest and engage the potential client and intervene with them. Treatments which participants in their natural environment, such as treatments delivered over the Internet or in neighborhood settings such as churches and recreation centers are desired.

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9. Development of HIV Risk Reduction Interventions. Research to develop and evaluate behavioral strategies to reduce HIV risk behaviors in HIV-positive and HIV-negative substance abusing treatment populations. Risk reduction interventions should be specially adapted to patients' age, gender, cultural background and potential cognitive impairments and should address compliance with medical regimens. The product of such research might be educational materials, such as manuals or videotapes that describe the intervention and its implementation by treatment staff.
10. Complementary and Alternative Therapies (CAT) for Drug Abuse Treatment. Research is encouraged on complementary and alternative interventions for drug abuse

treatment. CAT interventions could be the sole treatment or could be adjunctive strategies to enhance the therapeutic potency of existing drug abuse treatments. An example of an adjunctive CAT intervention might be where the intervention reduces withdrawal symptoms thus enhancing retention in treatment. Included would be interventions that are commonly used in "real world" treatment settings, but whose therapeutic efficacy has not been scientifically demonstrated. Such interventions include acupuncture, bioelectrical stimulation, exercise, biofeedback, meditation, among others. The product of this research might be a manual or video, which illustrates the intervention and how it is implemented by treatment staff.

11. Incorporating Smoking Cessation in Drug Abuse Treatment. Research is encouraged to develop and test behavioral treatments for nicotine-addicted individuals who also are addicted to other substances, such as heroin, cocaine, methamphetamines and alcohol. Prevalence of cigarette smoking is extremely high among drug dependent individuals attending drug treatment. Many treatment providers are reluctant to address smoking cessation with clients either because they believe that substance abusers are not interested in quitting or because they fear smoking treatment will have a negative impact on drug abuse treatment outcome. However, studies have shown that many drug abuse clients are interested in quitting smoking and that the concurrent treatment of tobacco dependence and other drug dependencies does not threaten abstinence and might even assist in maintaining it. Research is needed to develop and test smoking cessation treatments that can be incorporated into treatments for illicit drugs of abuse.
12. Developing Treatments for Smokers with Co-morbid Disorders. Research is encouraged that focuses on the development, refinement, and testing of behavioral treatments for smokers with psychiatric co-morbidity, such as depression, schizophrenia, or anxiety disorders. Smoking prevalence is very high in individuals with psychiatric disorders.

These populations generally respond poorly to traditional smoking cessation treatments. Research is needed to develop and test innovative behavioral and combined behavioral and pharmacological treatments that address the unique needs of these individuals.

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13. *Development of New or Improved Addiction Assessment Measures and Procedures.*

Research directed at the improvement of a currently available measure or the design of a new psychosocial, social or environmental measure appropriate for use in the clinical assessment of substance abusing populations. Special consideration should be given to a specific screening or diagnostic tool, or to a specific measure of treatment readiness, treatment compliance, service utilization, therapeutic process or drug treatment outcome. The scope of the study might cover the establishment of the instrument's reliability (e.g., inter-rater; test-retest; item-analysis), validity (e.g., discriminant; construct; concurrent; predictive), sensitivity/specificity, a normative data set for a specific clinical population, a standardized form of administration, different response formats, a specific language version other than English, and/or the instrument's utility in different clinical settings.

14. *Behavioral Therapies for Pre-Adolescents and Adolescents.* Behavioral therapies for pre-adolescents and adolescents that incorporate HIV risk reduction counseling as an integral component of the treatment. This includes the development of new, or refinement of existing psychotherapies, behavioral therapies, and counseling (group and/or individual). This also includes the development and testing of manuals as well as other creative, interactive approaches for therapy delivery that may consider different settings for delivery, such as primary care, school-based health programs, juvenile justice settings, etc. Also the behavioral treatments should be culturally and gender sensitive.

15. *Behavioral Therapies for Couples and Families.* This includes the development of

new psychotherapy approaches, the modification or testing of existing behavioral treatments, and the design and/or testing of innovative clinical training and supervision methods for dissemination of efficacious treatments to community settings. Treatments that target domestic violence or other forms of interpersonal abuse along with substance abuse are encouraged.

16. *Behavioral Therapies for Groups.* This includes the development of new psychotherapy approaches, the modification or testing of existing behavioral treatments, and the design and/or testing of innovative clinical training and supervision methods for dissemination of efficacious treatments to community settings. Examples of relevant projects are: traditional group therapies, such as 12-step and therapeutic community approaches, and newer group therapies such as cognitive-behavioral and acceptance-oriented approaches; groups for various populations, such as adolescents, adults, couple and family groups, gender-specific groups, and groups tailored for racial or ethnic minority populations. Of particular interest are projects that address the recent findings suggesting possible contraindications of group treatments for some populations (e.g., delinquent adolescents), or in some formats (e.g., less-structured, emotion-focused group treatments).

17. *Behavioral Therapies Drawing from Stress Research or Stress-Management Interventions.* Projects are encouraged that apply concepts from stress research (such as appraisal, coping, and social support) to drug abuse in innovative ways, or that test the extent to which stress-management interventions can be applied to the treatment of drug abuse and interventions to reduce risk of HIV and other infectious diseases. Examples of stress-management techniques that may have novel application to drug abuse and HIV risk include techniques that teach problem-solving and affect-management, restore one's sense of purpose and meaning, prevent burnout in the face of chronic stressors, increase self-efficacy for managing stress, inoculate against stressors, train relaxation and

meditation, intervene during crises, enlist social support and system support, and others.

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18. *Modifying Efficacious Behavioral Treatments to be Community Friendly.* Several behavioral interventions have been found to be efficacious for the treatment of drug addiction. However, there are barriers to implementation of behavioral therapies in community-based settings. Community settings that treat drug addicted individuals are reluctant or unwilling to adopt these interventions for a variety of reasons. Reasons that scientifically-based behavioral treatments are not accepted by community providers could include the excessive cost of implementation, the length of time for administration of treatment, inadequate training available for therapists and counselors, treatments not shown to be generalizable for different patient populations or for polydrug abusing populations, etc. Research aimed at modifying efficacious behavioral treatments to make them more acceptable to community settings is needed. Settings might include, drug abuse treatment facilities, primary care, managed care, and the criminal justice system. Examples of possible studies are those that are designed to reduce the cost of implementation of treatments, reduce the time of administration of treatments, aid in training of therapists, counselors and nurses, adapt individual therapies for group situations, etc.
19. *Innovative Technologies for Drug Abuse Treatment, HIV Risk Reduction, and Training Clinicians.* Relevant research would be directed at the development and evaluation of innovative technologies to treat substance abuse, enhance adherence to medications, and/or reduce risk for HIV infection or transmission. Approaches should be capable of being readily incorporated at reasonable cost into various treatment settings. Areas of interest include Internet-based treatment or training programs, CD-ROM technology, audio delivery devices, photo therapeutic

instruments, and hand-held computers. Also of interest are creative approaches for disseminating science-based behavioral treatments and for training therapists to use scientifically based treatments for drug abuse and addiction. Such approaches might include Internet-based education, interactive computer programs, telemedicine, etc. Finally, approaches which apply therapies with evidence of efficacy through new media such as web-based platforms, over email, or through chat rooms and bullet boards are also desirable.

20. *Virtual Reality Applications for Drug Abuse Treatment Provider Training.* Recently virtual reality simulations have been used to train medical personnel in demanding medical procedures such as microsurgery techniques. Virtual training allows trainees to gain familiarity with both the environment in which services are delivered as well as the intervention techniques without the danger of mistakes impacting live patients. Virtual reality interfaces can assess skill acquisition and provide detailed feedback during procedures to help trainees correct mistakes or avoid making them altogether. In the drug abuse field, training and dissemination efforts have been hampered by a dearth of knowledge about ways to conduct dissemination. Although trainees often practice on actual clients, this approach has drawbacks including its reliance on the client or participant's schedule and willingness to participate in training sessions and potential danger to the client or if the intervention is delivered incorrectly. Libraries of virtual reality simulations of drug users in treatment or "virtual patients" are needed to provide experiential training for treatment providers without relying on existing patients. This will help facilitate the rapid and effective dissemination of proven treatment strategies.

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- D. *Clinical Neurobiology Branch (CNB).* The CNB supports research on the biological etiology (determining the biological basis for vulnerability to drug abuse and progression to



addiction, including studies on individual differences and genetics) and clinical neurobiology of addiction (exploring alterations of the structure and/or function of the human central nervous system following acute or chronic exposure of drugs of abuse), and the neurobiology of development (neurobiological effects of drugs of abuse and addiction during various stages of development and maturation, effects of drug exposure on neurobiological processes, development of methodologies and refinement of techniques used in pediatric neuroimaging). The Branch also supports investigations on the cognitive neuroscience of drug abuse and addiction, the neurobiology of treatment, neuroAIDS, and human pain and analgesia. Areas that may be of interest to small businesses include, but are not limited to:

1. *Development of Novel Approaches in Human Neuroscience*. Development of innovative, noninvasive research methods or novel approaches are needed to identify various neurobiological markers of brain alterations in humans induced by acute or chronic exposure drugs of abuse. This may include the identification of neurobiological (including genetic) markers that might be associated with risk for, or resilience to drug abuse and addiction. Of particular interest are noninvasive methods (e.g., brain imaging) that could be used to determine the effects of drug abuse/addiction treatments on neurobiological systems in an attempt to understand the neurobiological processes underlying therapeutic efficacy.

In recent years, there has been an increase in studies employing functional magnetic resonance imaging (fMRI) to understand brain processes and functional neuronal systems. In particular, these neuroimaging techniques are being used to probe how drugs of abuse alter brain functioning. Consequently, there is a need for the development of stimulus generation hardware to be used within an fMRI magnet that can display stimuli important in drug studies. As the studies of brain function become more sophisticated, task-related assessments of brain activation are increasingly important. Shielded goggles or other types of stimulus-generating hardware and software are necessary for presentation, for example, of

neurocognitive tasks, drug-related images for the induction of craving, or other “virtual reality” types of dynamic stimuli important in studies of drug abuse and addiction. Responses to this type of stimulation then could be correlated with brain measures using neuroimaging techniques. These types of studies will provide new insights into drug-brain-behavior interactions.

Development of the human central nervous system and how drugs of abuse perturb this process is of great interest. Little is currently known about the effects of exposure to drugs of abuse, either prenatally or during childhood or adolescence, on the development of the human nervous system. Further, the application of newly emerging technologies (such as neuroimaging) to these populations presents unique challenges due to the fact that the central nervous system, and its capabilities, are changing rapidly. The development of novel techniques, or the refinement of existing methods, to provide direct noninvasive measures of brain structure and/or function that are adapted specifically for use in pediatric and adolescent populations is strongly encouraged. Also, neurocognitive and other neurobehavioral tasks for use in these populations, especially where they can be designed to probe underlying neurobiological processes, need to be developed.

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2. *Virtual Reality for the Neurobiological Study of Drug-Brain-Behavior Interactions and Drug Abuse Treatment*. Virtual Reality (VR) is an emerging technology useful in a variety of research-related, therapeutic and instructional settings. By immersing a person's senses in a synthetic world or Virtual Environment (VE) that characterizes VR, a highly flexible and programmable set of stimuli can be used to enhance the standard approaches used in assessment



of neurobiological and neurobehavioral processes.

Collection of real-time data and bulk data recording can provide a correlation of a stimulus reference signal with simultaneously collected fMRI scanner and physiological data over time. Unlike most computer access systems that accept only one or two modes of precise and/or discrete input at a time, VR systems have the potential to monitor movement or action from any, or many, neurobiological functions at once. In addition, the multimodal feedback inherent in VR provides a way to vary nonvisual stimulus components (e.g., resistance, temperature, pitch) in a way that is impossible to achieve via standard computer systems. Finally, VR systems provide a bypass for keyboard entry or direct manipulation environments (e.g., pointing instruments like the mouse), by allowing the manipulation of multi-sensory representations of entire environments by natural actions and gestures.

VE can provide a completely controlled, noninvasive, safe and alternative methodology for a variety of important studies of drug abuse and addiction. For example, VR allows for the presentation of a variety of complex, multi-sensory stimuli for neurocognitive tasks or, alternatively, the dynamic stimuli important for producing drug-related images for the induction of craving. VR can also be tested as an alternative to traditional behavioral therapies in the treatment of drug abuse. Responses obtained as a result of the above can then be correlated with brain measures using state-of-the-art neuroimaging techniques. We, therefore, invite studies employing VR, especially to probe brain processes in drug abuse/addiction combined with neuroimaging methods or to be developed or applied as a potential treatment for substance abuse.

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3. *Development of Interactive Computer Applications for Neuropsychological/ Neurocognitive Assessment to Determine*

*Functional Brain Deficits in Acute and Chronic Drug Abusers.* In addition, a neurobehavioral test battery to assess other neurobehavioral/ neurocognitive deficits resulting from drug abuse/addiction is encouraged. Of particular interest is the development of such assessments for use in children and adolescents exposed to drugs of abuse to better define and understand the effects of early exposure on brain function and development (for developmental issues, contact Larry Stanford, Ph.D.).

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4. *Development of Ligands for Brain Imaging.* Development of novel radioligands for PET and SPECT imaging in human brain for molecular targets (e.g., receptors, intracellular messengers, disease-related proteins) is of broad interest to the neuroscience and drug abuse research community. The primary application of these radiotracers will be in basic neuroimaging research. Ultimately, these radiotracers may also be used as potential biological markers and surrogate endpoints for translational and clinical research, drug discovery and development, and clinical trials. The scope of the projects may encompass pilot or clinical feasibility evaluation in pre-clinical studies, model development, or clinical studies. Alternatively, the focus may be on research and development of new technologies for radiotracer development.

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- E. *Medications Research Grants Branch (MRGB).* The MRGB supports investigations of the use of medications for the treatment of drug abuse and dependence disorders, with the aim of assisting addicts to reduce illicit drug use, become drug free, prolong abstinence, decrease associated psychosocial, medical or

legal problems, or survive drug overdose. In general, pharmacotherapies are expected to be added to a platform of appropriate behavioral therapy. The program funds extramural grants in the following areas:

- Controlled clinical pharmacological studies to assess a compound's potential as a drug abuse/dependence treatment medication.
- Controlled clinical trials for the assessment of new agents, or new indications for marketed agents, for the treatment of drug abuse or its complications (withdrawal, relapse, overdose).
- Clinical studies of the pharmacological effects and interactions among experimental addiction medications, the various substances abused by drug-dependent individuals, and other medications used for associated psychiatric and medical conditions.

Areas that may be of interest to small businesses include, but are not limited to:

1. *Pharmacogenetics and Substance Use Disorders*. The emergence of new genetic techniques may allow the use of genetic information to improve the safety and efficacy of treatments. The field of pharmacogenetics focuses on the genetic determinants of response to medications and other in humans and animals. The goal is to discover novel single nucleotide polymorphisms (SNPs) and test their relevance to the underlying genetic differences that determine the safety and efficacy of medications for the treatment of SUD. It includes the study of genes encoding drug metabolizing enzymes, transporters, receptors and other drug targets, polygenic determinants of drug disposition and effects in humans, the role of genes in the clinical response to and medical safety of medications, and application of genetic information to disease prevention and to optimize treatments in humans. It also includes novel methods for phenotyping the diagnosis, safety and treatment outcome of SUD. Ultimately, it is expected that pharmacogenetics research will help clinicians to individualize the treatment of their patients based on their genetic

information. Research is needed to study the genetic factors that may be associated with drug abuse treatment safety and outcome.

2. *Medications Development for the Treatment of Drug Abuse in Adolescents*. Drug abuse among adolescents is a significant and growing public health concern. It is known that the pharmacokinetics and pharmacodynamics of some medications are different in adolescents. Therefore, adolescents may present overdoses, underdoses or lack of efficacy, or different safety profiles when administered medications at the doses studied only in adults. Unfortunately, little is known about the safety and efficacy of medications for the treatment of drug abusing adolescents because most of the drug abuse medication research has focused on adults. Research is needed to test medications for the treatment of nicotine and drug abuse in adolescents.
3. *Medications for the Treatment of Pregnant and Post-Partum Drug Abusing Women and Their Children*. Little is known about the safety and efficacy of medications for the treatment of substance abusing pregnant women and their children. There is a need for safe and effective medications for the treatment of nicotine and drug abuse among pregnant and post-partum women and the effect of the medications on their children. Research is also needed to study the effects on the newborn of the medications taken by the mother and medications for treatment of children born to substance abusing mothers who may present drug withdrawal and other symptoms.
4. *Medications for the treatment of comorbid medical or mental disorders and drug abuse*. Co-morbid medical and psychiatric conditions are frequently found among substance abusing patients. Co-occurring mental disorders, such as depression, post-traumatic stress disorder, and anxiety disorder, and medical conditions such as hepatitis C, AIDS related disorders, and pain, are common among substance abusing patients.

Unfortunately, there are presently no commonly prescribed safe and effective

medications for the treatment of substance abusing patients with other co-morbid medical and psychiatric conditions. Research is needed to study the safety and therapeutic profiles of medications for treatment of substance abuse in patients with other comorbidities. There is also a need to study the effects of medications for the treatment of substance use disorders in patients taking medications for other comorbid conditions and the necessary dose adjustments.

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### **Division of Neuroscience and Behavioral Research (DNBR)**

DNBR's basic neuroscience and behavioral research focuses on understanding the mechanisms, characteristics, and processes of drug abuse. Basic behavioral, cognitive, neurobiological, cellular, molecular, chemical, and genetics research aims at characterizing and understanding drug seeking, compulsive behavior, and addictive processes. These research areas necessarily include studies of normal processes.

Using both animal and human studies, basic behavioral research focuses on behavioral and cognitive processes that may or do lead to drug initiation, and the behavioral and cognitive consequences of drug abuse. Neurobiology research focuses on the neural mechanisms and substrates underlying behavioral and cognitive processes and vulnerability factors associated with drug abuse, addiction, sensitization, tolerance, and relapse.

DNBR supports basic chemistry and pharmacological studies focusing on structure/activity relationships, definition, and characterization of systems involved in drug actions, chemical synthesis of new ligands, pharmacokinetics, analytical methods, understanding basic mechanisms of drug action and drug testing.

Computational and theoretical modeling of biological systems and behavioral processes, biomedical computing and/or information science and technology development is supported by DNBR.

- A. **Research Related to the Design of New Therapeutic Approaches.** Development of new therapeutic approaches based on the application of nanoscale particle formulations for drugs that are either poorly water-soluble or otherwise unstable under physiological conditions, and development of methods for using nanoscale formulations for targeting specific brain sites or to control drug delivery over extended periods of time.

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- B. **Virtual Reality for Treatment of Pain.** Recent findings (Hoffman et al., 2000, Pain, 85, 305-309) have suggested that Virtual Reality (VR) exposure can reduce reported pain during wound care. Grant proposals are sought to examine the utility of VR technologies in the treatment of various types of pain. Development of treatments for both acute and chronic pain are sought. These treatments can be based in clinical settings or the patient's homes. Phase I testing should establish the feasibility of the use of this technology in the particular population to be tested. Phase I should also produce data that demonstrates that this methodology is effective for the particular type of pain being treated. Phase II should involve larger-scale testing (e.g., more subjects and treatment trials) examining various treatment parameters (e.g., timing of treatment, types of VR environments). The focus of Phase II testing should be the refinement of this treatment for use in pain patients.
- C. **Virtual Reality for the Treatment of Drug Abuse.** Recent findings (Hoffman et al., 2000, Pain, 85, 305-309) have suggested that Virtual Reality (VR) can be a useful clinical tool. In this particular study, VR exposure was used to allow patients to selectively not attend to an otherwise painful procedure. Drug abuse, like pain, is a problem that is strongly impacted by stimuli in the abuser's environment and psychological factors. Thus, it is reasonable to assume that VR may be useful in allowing individuals to ignore drugs cravings, withdrawal symptoms or environmental cues that promote drug abuse. Grant proposals are sought to examine the utility of VR technologies in the treatment of various types of drug abuse. These treatments can be based in clinical

settings or the patient's homes. These treatments can be developed to address drug withdrawal, drug craving or on-going drug related behaviors. The development of VR technologies to address abuse of all types of drugs (e.g., cocaine, marijuana, nicotine, alcohol, inhalants) are sought. Phase I testing should establish the feasibility of the use of this technology for the particular drug problem addressed (e.g., cocaine craving, opioid withdrawal) and should also produce data that demonstrates that this methodology is effective for the particular drug problem. Phase II should involve larger-scale testing (e.g., more subjects and treatment trials) examining various treatment parameters (e.g., timing of treatment, types of VR environments). The focus of Phase II testing should be the refinement of this treatment for use in the treatment of drug abusers.

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D. **Chemical Libraries for Drug Development.**

The development and biological screening of lead compounds and their combinatorial libraries for use in the area of drug abuse treatment research are encouraged, such as generation of new ligands having opiate receptor selectivity, or ligands with NMDA or serotonergic agonist/antagonist activity and/or related. These are designed as lead compounds either for drug design or as tools to elucidate mechanisms of action of drug abuse.

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E. **G Protein Coupled Receptor Monitoring.**

The National Institute on Drug Abuse supports research on wild type and mutant G protein coupled receptors (GPCRs) such as the opioid, cannabinoid, and orphanin receptors. There is current interest in the cellular dynamics of these receptors, including the processes of activation by various ligands, internalization and recycling, oligomerization, phosphorylation/dephosphorylation, and degradation. In this respect, phase I and combined phase I/II applications are sought in these areas:

1. Development of new fluorescent reagents for conjugation to receptor proteins and

their fragments, including quantum dot conjugates and laser-excitabile dyes for long visible-near infrared range emission (650-900nm), for use with various technologies, including internal reflectance fluorescence microscopy and confocal microscopy, and protein detection with capillary electrophoresis.

2. Development of expression systems for the production of beta-arrestins and G protein coupled receptor kinases tagged with green fluorescent protein, or its mutants and variants.

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F. **Genetic Studies.** The National Institute on Drug Abuse is interested in SBIR proposals that would greatly facilitate the identification of genetic loci that confer vulnerability to substance abuse and addiction. Areas of interest include but are not limited to:

1. Collection and genotyping of human pedigrees and sib-pairs for vulnerability or resistance to drug abuse.
2. Isolation and identification of mutant strains in genetic model systems such as Zebrafish, Drosophila, C. elegans, mice, and rats that are more vulnerable or resistant to drugs of abuse.
3. Design, development, and marketing of behavioral apparatuses to conduct rapid behavioral throughput screens for identifying genetic vulnerability to addiction in genetic model systems.
4. Development of transgenic models for drug abuse using bacterial artificial or yeast artificial chromosomes.
5. Development of software and databases for candidate genes for drug abuse.
6. Identification and mapping of functional polymorphisms of candidate genes for drug abuse.
7. Placement of candidate genes for drug abuse on biochips.
8. Marker-assisted breeding of congenic mouse and rat strains for mapping quantitative trait loci associated with addiction and drug abuse.

## 9. Vectors for gene transfer into neurons.

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- G. **Drug Testing Development.** Development of new, more refined or more practical drug testing methodologies. Studies may focus, but are not limited to the following topics: drug testing methods; drug extraction procedures; methods to control for possible environmental contamination factors; and reference materials. Methodologies with special application to the workplace, the emergency room, the transportation environment, or other specific settings are welcome. Methodologies with an emphasis upon circumstances for testing such as post-accident testing or readiness for work testing are also encouraged.

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- H. **Effects of Drugs at the Cellular Level.** Development of new imaging techniques, reagents and related hardware and software for dynamic investigations of the effects of drugs of abuse on cellular activities and communications. For example, these techniques might include, but are not limited to, development and utilization of reagents for magnetic resonance microscopy and other MRI methods; development of methodologies applying functional MRI to drug abuse studies; the use of dyes, intrinsic signals, and other optical indicators for studying signal transduction mechanisms, the regulatory control of protein entities (such as phosphorylation), and neuronal excitatory and inhibitory pathways. Areas of interest may include, but are not limited to:

1. Studies using molecular biological techniques to scale-up protein production for investigations aimed at enhancing understanding of the structure, function and regulation of molecular entities involved in the cellular mechanisms through which abused drugs act.
2. Validated in vitro test systems can reduce the use of animals in screening new compounds that may be of potential benefit in treating drug abuse. Test systems are needed to evaluate activity at receptors or

other sites of action, explore mechanism(s) of action, and assess potential toxicity.

3. With the recent success in molecular cloning of various drug abuse relevant receptors, enzymes, and other proteins, researchers will elucidate the molecular mechanism of action of these drugs. Studies to generate strains of transgenic animals carrying a gene of interest are solicited. Of special interest are knockout and tissue-specific knockout animals. These animals can be used to identify gene function, and to study the pharmacological, physiological, and behavioral role of a single gene.

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I. **Toxicity Studies**

1. Studies on abused drugs and their metabolites to develop methodologies that may be potentially useful in addressing medical emergencies. Such studies might include investigations involving development of pharmacokinetic models, methodologies, and data.
2. Concern remains about the potential acute and chronic neurotoxicity of drugs of abuse. Information is needed about the possible neurotoxicity of pharmacotherapeutic agents with potential for treating drug abuse. Improved methods are needed for identifying, assessing, and quantifying the nature and extent of neurotoxicity. Such studies might include the development or application of quantitative chemical, physiological, or behavioral measurements relating to nervous system injury or methods for quantitative analysis of damage.

- J. **Predisposition to Cardiovascular Complications Associated with Abused Substance(s).** Development of experimental animal models to assess a genetic predisposition or increased sensitivity to cardiac and vascular complications associated with drug use. Such studies might include, but are not limited to, investigations involved with biochemical, physiological and pathological indices of cardiovascular system function.



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K. **Opioid Peptides.** Research and development directed at the medicinal chemistry and molecular pharmacology of opioid peptides, especially in methods development. Areas of interest include but are not limited to:

1. Development of innovative methodologies for the synthesis of opioid peptides to be made available to researchers. Syntheses proposed should be limited to single analogs.
2. Methods to identify new ligands for opioid receptors and the design of new opioid peptide analogs with therapeutic potential.
3. Development of analytical methodologies for the quantitation of synthetic and endogenous opioid peptides, peptide precursors, and processing enzymes. The innovation may be limited to a part of the method, such as development of a special detector or a sample cell. Methods might include antibody development and development of innovative immunoassays.

L. **Dopamine and Serotonin Receptor Ligands.** Both dopamine and serotonin receptors exhibit multiple subtypes. Applications are solicited using chemical combinatorial library techniques to develop ligands having a high degree of selectivity to these receptor subtypes, which can be useful both as pharmacological tools and lead compounds in medicinal chemistry/drug development.

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M. **Systems Biology.** The National Institute on Drug Abuse is interested in SBIR proposals that would facilitate global analysis of biological systems relevant to drug abuse. Technologies and resources developed should be applicable and relevant to drug abuse research. Areas of interest include, but are not limited to:

1. Improved technology for analysis of membrane proteomes for the identification of targets and validation of leads.
2. Development of technology or new strategies that will improve dynamic range

to allow the analysis of a broader spectrum of the proteome of neural cells.

3. Single cell analysis and the development of model systems for proteomic analysis of neuronal function and drug effects.
4. Development of real-time proteomics technology for the analysis of processes such as cellular responses to drug exposure.
5. High throughput, high resolution 3-dimensional in situ proteome profiling such as optical projection tomography, improved methods for high throughput sectioning of neural tissue and the development of tools for identifying and mapping protein expression, localization and movement relevant to addiction and other medical consequences of drug abuse.
6. High throughput, functional, molecular interaction screening methods for proteins implicated in drug abuse.
7. Strategies to characterize post-translational modifications related to addiction and drug effects.
8. Development of proteomic tools for identifying biomarkers to track therapeutic efficacy, to monitor effects of drug interactions, and to advance biological understanding of relationships between drug use and infectious disease, and therapies for HIV, hepatitis C and other diseases.
9. Development of computational tools such as knowledge bases, information systems and computational models for protein data related to addiction and other medical consequences of substance abuse. Tools that enable the integration of proteomics, genomics, transcriptomics, metabolomics and other data into applications leading to systems understanding of drug effects upon biological systems.
10. Technologies to identify parameters of molecular, cellular, or physiological systems important in addiction, and the properties of the system, such as redundancy and robustness.
11. New approaches for characterizing cell phenotypes and mapping those phenotypes.



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N. **Research Resources.** The National Institute on Drug Abuse is interested in SBIR proposals that would generate the following resources for drug abuse research:

1. Resources for the application of genetic engineering to dynamically monitor neuronal function.
2. C57BL6 Mouse embryonic stem cells and spermatogonial stem cells.
3. Turnkey technology for proteomics such as the development of protein and peptide chips to study drug effects on neuronal mechanisms.
4. Antibodies, aptamers, ligands, etc. relevant to drug abuse research.

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O. **Development of Innovative Pulmonary Nicotine Delivery Systems.** NIDA is seeking SBIR grant applications for development of devices that achieve the pulmonary delivery of nicotine in human subjects. A major effort in smoking cessation centers on nicotine replacement. Pulmonary delivery of nicotine should permit more reliable replication of the delivery that occurs during the inhalation of tobacco smoke. Thus, such devices would prove valuable as resources in support of research studying the efficacy of rapid nicotine replacement, and as potential future aids in smoking cessation. The devices should be small, portable, and deliver a "smoking-dose" of nicotine in a reliable manner.

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P. **Development of Innovative Synthetic Probes, Drug Dosage Forms, and/or Drug Metabolites For Drug Abuse Research.** Proposals are solicited for the synthesis of new

chemical compounds, drug metabolites, peptidomimetics, and/or development of drug dosage forms for studying the mechanism of action of drugs of abuse and drug addiction.

Specifically proposals are encouraged in the following areas:

1. Synthesis of chemical probes, drug metabolites, peptidomimetics, and/or development of drug dosage forms that are needed by drug abuse research investigators, and they are not commercially available, and/or available with great difficulty.
2. Alternate synthetic methods for existing chemical probes that improve the yield and produce these chemicals at lower costs as compared to commercially available substances.
3. Development of alternate drug dosage forms of existing drugs/drug products for enhancing their efficacy.

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Q. **Development of Analytical Techniques.** The development of new analytical methods for measuring drugs of abuse and their metabolites in biological matrices, such as urine, blood, saliva, sweat, hair, breast milk, brain tissue, and meconium is encouraged. The new methods should be efficient, sensitive, convenient, and cost effective. Modifications and improvements in existing analytical techniques are also encouraged particularly those improving sensitivity and selectivity.

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## **Office of Science Policy and Communications (OSPC)**

### **SCIENCE POLICY BRANCH (SPB)**

**Science Education.** In order to improve science education in the area of drug abuse research (e.g., disciplines such as neuroscience, psychology, epidemiology), efforts are needed to develop innovative methods for improving knowledge of and generating interest in science among school children, the general public, and health care

providers, including providers involved in drug abuse treatment. These might include but are not limited to:

- A. Development of methodologies to present drug abuse and science information to particular groups, such as kindergarten and elementary school students, African Americans, Hispanics, persons with disabilities and health care providers.
- B. Development of methodology to transfer new knowledge and directions of scientific growth to teachers, curriculum developers and health care providers.
- C. Development of computer-based learning systems that allow students to experience the scientific process.
- D. Development of specific materials, activities, or programs that promote science education related to drug abuse, such as exhibits, curriculum materials, coloring books, videos, teacher education workshops, partnership programs with scientists and educators, or workshops for health care providers.
- E. Development of specific materials, activities or programs that promote the teaching of scientific and research ethics to middle and high school students.

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#### **Division of Epidemiology, Services and Prevention Research (DESPR)**

- A. **Prevention Research Branch (PRB).** The Prevention Research Branch (PRB) supports a program of research in drug abuse and drug related HIV prevention to (1) examine the efficacy and effectiveness of new and innovative theory-based prevention approaches for drug abuse, drug-related HIV/AIDS and other associated health risks, (2) determine the cognitive, social, emotional, biological and behavioral processes that account for effectiveness of approaches, (3) clarify factors related to the effective and efficient provision of prevention services, and (4) develop and test methodologies appropriate for studying these complex aspects of prevention science.

**Prevention Research.** Rigorous scientific prevention research is encouraged to study novel approaches to substance abuse prevention for use at multiple levels of the

social environment including: the family, schools, peer groups and organizations, the workplace, health care systems, etc. The purpose of this research is to determine the efficacy and effectiveness of novel program materials, training strategies, and technologies developed to prevent the onset and progression of drug abuse and drug-related HIV/AIDS infection. Materials and technologies may entail a comprehensive approach encompassing audiences at the universal, selective, and/or indicated levels. Universal interventions target the general population; selective target subgroups of the population with defined risk factors for substance abuse; indicated interventions target individuals who have detectable signs or symptoms foreshadowing drug abuse and addiction, but who have not met diagnostic criteria. NIDA encourages the development and testing of innovative prevention intervention technologies that are sensitive and relevant to cultural and gender differences.

1. Laboratory studies of the underlying mechanisms and effects of various prevention approaches such as persuasive communication (e.g., mass media and print media) as they are affected by and affect on drug related cognition, emotion, motivation and behaviors.
2. Decomposition of prevention programs to understand components that account for program effectiveness.
3. Research on design features of prevention curricula, materials, and approaches that result in positive outcomes.
4. Training modules for program implementers of research based substance abuse prevention programming strategies.
5. Prevention intervention dissemination technologies and mechanisms that integrate research with practice; specifically the transfer of drug abuse prevention information to decision-makers, funders, and practitioners.
6. Prevention services research on the organization, financing, management, delivery, and utilization of drug abuse prevention programs.
7. Strategies for the integration of proven prevention approaches into existing service delivery systems.

8. Studies that develop and assess reliability and validity of developmentally appropriate self-report, physiological, and biochemical measures for use in prevention trials in a variety of settings and a variety of audiences.
9. Development of community needs assessment tools and services.
10. Drug abuse prevention methodological research on promising data collection, data storage, data dissemination, and reporting techniques.

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B. **Epidemiology Research Branch (ERB).** The ERB supports an extramural program for epidemiologic research concerning drug abuse which includes (1) incidence and prevalence of drug abuse (in various stages) and related conditions such as HIV/AIDS among general and specific subpopulations, (2) identification and study of resiliency and risk factors associated with drug abuse and related conditions, (3) etiologic studies on the origins and pathways of drug use during various stages of human development, (4) methodological studies designed to measure and improve the accuracy, collection, and reporting of data on drug abuse and related conditions, (5) development of innovative statistical approaches and research designs leading toward improved analysis of drug abuse characteristics, (6) international epidemiologic studies on drug use patterns, etiologic factors, and related concerns in various national and regional contexts.

1. **Assessment and Improvement of the Validity of Sensitive Data Collected in Drug Use Surveys.** The accuracy and validity of self-report of drug use and related behaviors and consequences in the context of epidemiologic surveys is a matter of great concern. Research is needed on various methods of survey data collection that assures more accurate reporting. Techniques such as those based on variations in standard survey protocols, and those based on use of computer-assisted self-interview (CASI) or computer-assisted personal interview (CAPI) methods are encouraged.

2. **Instrument Development for Assessing Community Factors that Affect Drug Use and its Consequences.** Essential to the assessment and analysis of the relationship between contextual/environmental, sociocultural factors, and health is the consideration of community milieu, as the social, physical and economic characteristics of the community context can have both short- and long-term consequences for community members' physical and psychological well-being. In order to elucidate this important connection between community characteristics and behavioral and social consequences of drug use, this announcement is soliciting applications for the development of community diagnostic instruments to facilitate psychometrically sound assessment of such factors. In this context, community is defined in its broadest sense to include social groups comprised of individuals who have formed attachments based on a variety of shared factors, such as, kinship, beliefs and values, race and ethnicity, and territory (e.g., neighborhood). Instruments are needed to provide local specificity on the physical characteristics as well as the characteristics of important social groups (including the dynamic nature of individuals involvement in such social groups). Such standardized assessments of community characteristics are needed to better understand the full impact of drug use on behavior and to develop targeted interventions to specific community needs.

The consequences of drug use and/or abuse in society take a profound toll on families, schools, and other community institutions and burden the criminal justice, health care, and social welfare systems. Consequences of interest include, but are not limited to, educational and occupational problems (illiteracy, school dropout, unemployment, job absenteeism and turnover), individual criminal activities (violence, vandalism, homicides, sexual abuse, delinquency), and poverty, homelessness, gang activities, drug trafficking and distribution systems, and family disruption and dislocation (family violence, divorce). Yet, research to enhance the understanding of how community factors affect the prevalence and incidence of such outcomes is

hindered by a lack of standardized measurement instruments to aid in defining and assessing critical community factors.

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- C. **Services Research Branch (SRB).** The SRB supports a program of research on the effectiveness of drug abuse treatment with a focus on the quality, cost, access to, and cost-effectiveness of care for drug abuse dependence disorders. Primary research foci include: (a) the effectiveness and cost-benefits and cost-effectiveness of drug abuse treatment, (b) factors affecting treatment access, utilization, and health and behavioral outcomes for defined populations, (c) the effects of organization, financing, and management of services on treatment outcomes, (d) drug abuse service delivery systems and models, such as continuity of care, stages of change, or service linkage and integration models, and (e) drug abuse treatment services for HIV seropositive patients and for those at risk of infection.

1. **Drug Abuse Treatment Economic Research.** This initiative will support research to design and develop data systems for financial management and economic analysis of treatment programs and larger systems in new healthcare settings and managed care networks. Managerial decision-making requires the implementation of sophisticated data systems to facilitate routine budgeting processes, allocation of resources, performance measurement, and pricing decisions. The focus is on the needs of managers within the organization and managers outside of the organization. Data system development must be based on standard cost behavior and profit analysis. Data systems must be designed with correct cost concepts (accounting and economic) in order to permit cost and pricing decisions to be developed for new treatment technologies and management of on going systems. In research settings, such an initiative is vital for the assessment of new technologies developed for transfer to practice.

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2. **Personnel Selection Technology Research for Drug Abuse Treatment Clinics.** NIDA would be interested in supporting small innovative research that develops and validates generic selection systems that could be adopted and tailored for use by drug abuse treatment clinics. Like many small businesses, drug abuse treatment clinics have problems attracting and retaining qualified personnel. Also like many small businesses, treatment clinics have limited resources to apply to the recruiting and hiring of new and replacement personnel. Though reliable data are lacking, a great many clinic directors complain of high annual staff turnover rates. This has been attributed anecdotally to poor quality of work life, low wages, low skill levels, incompatibilities with the clinic's treatment philosophy, and the high stress of working with drug abusers. Research has shown that the application of standardized selection methods designed to maximize person-job fit can cost-effectively reduce staff turnover. Systematic methods such as background inventories, protocol-driven interviews, aptitude tests, and credit checks have demonstrated validity for improving person-job fit. Examples of possible projects might include development of easy-to-understand guidance about legal considerations in hiring practices, software that transform job task analysis into selection criteria, interview protocols to standardize applicant screening, tolls to help improve recruitment, and/or self-paced training for hiring officials or interview panels to improve screening reliability.
3. **Customer Retention Technology.** Premature disengagement from drug abuse treatment participation is a common problem and ranges from approximately 30 to 60% based upon the clinic and modality studied. Past research has very frequently attributed dropping out of treatment to participant characteristics (e.g., motivation, addiction severity, co-morbidity) and/or environmental factors (e.g., social pressures, unemployment, homelessness). Seldom has the dropout problem been studied in the context of customer satisfaction. That is, there is little research



looking at the causes of dropping out of treatment attributable to organizational factors (e.g., policies, practices, context) that influence participant withdrawal decisions. Needed are tools and system for assessing and survey drug abuse treatment program participant perceptions and satisfaction levels, summarizing and report participant assessments, interpreting results and adjusting policies and practices to improve satisfaction and participant retention in treatment.

4. *Effective Management and Operation of Drug Abuse Treatment Services Delivery.*

The bulk of drug abuse treatment is conducted in small clinical settings with therapeutic staffs of less than a dozen people. Small clinics lack resources to help improve efficiency and effectiveness in both business and therapeutic practices. Areas that may be of interest to small businesses include, but are not limited to:

- a. Computer-based leader/manager self assessment tools to enable those supervising the delivery of drug abuse treatment services to gain insights about strengths and weaknesses, and to help guide them to improved leadership and management practices.
- b. Organizational change tools: Handbooks describing step-by-step way to introduce more efficient business practices such as quality management/monitoring, creating empowered work teams, formalized goal setting, improved customer relations, forming organization linkages, and adopting new fiscal and resource management techniques.
- c. Organizational change tools: Handbooks describing step-by-step ways to introduce more efficient or effective therapeutic practices such as, adding pharmacotherapy in a previously drug-free clinic, adopting new medical/pharmacotherapy or behavioral interventions, and adopting new approaches to clinical collaboration and/or case management.

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5. *Web-Based Technologies: Transporting Services Research to Practice.* This initiative will support the development and testing of the effectiveness of web-based technologies that facilitate the translation of drug abuse prevention and treatment services research into practice. The ultimate goal is the delivery of efficacious, low-cost interventions to the greatest number of individuals in community settings. Delivery of evidence-based services in community settings often is hampered by lack of state-of-the-art information about the contents of efficacious interventions, the organizational structures and processes that make effective implementation possible, and available training and technical assistance. Applications may include, but are not limited to, the development and testing of new and innovative Internet-based systems that provide practitioners with (a) current information on evidence-based treatments with the greatest promise for defined populations of drug abusers; (b) assistance in translating clinical trials data into clinically useful information; (c) information and training on how to effectively organize, manage, and deliver evidence-based prevention and treatment services; (d) strategies for organizational change and capacity building; and (e) access to training and technical assistance on the adoption of new prevention and treatment interventions.

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**Center on AIDS and Other Medical Consequences of Drug Abuse (CAMCODA)**

The Center on AIDS and Other Medical Consequences of Drug Abuse (CAMCODA) develops and administers a national and international program of research on HIV/AIDS and other medical/health, mental health, and developmental consequences of drug abuse. CAMCODA also coordinates research activities, and collaborates with other NIDA components, on issues concerning HIV/AIDS and consequences of drug abuse.

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A. **Develop Improved Technology for Assessment of Prenatal Drug Exposure and Passive Postnatal Drug Exposure**

1. Develop and refine methods for the detection and quantification of infant exposure to drugs of abuse during pregnancy, including cocaine, marijuana, opiates, and methamphetamines.
2. Develop and refine methods for the detection and quantification of passive exposure to illicit drugs during infancy and childhood.

B. **Develop Interactive Database Systems on Human Subjects Issues for Use by Drug Abuse Researchers Studying School-Age Children and Adolescents Drug Use.**

Develop systems to assist investigators in obtaining technical and legal information relevant to involvement of children and adolescents in research on drug abuse. Examples of pertinent situations include tracking long-term health and development of children exposed to drugs during pregnancy, and investigating vulnerability and possible pathways to drug abuse among school-age children and adolescents. These database systems should address issues such as assent and consent, should provide information on variation in laws and guidelines across jurisdictions, should include the capacity for interactive communication on numerous situations potentially facing investigators, and should serve as sources of referral for additional assistance.

C. **Develop Improved Methods of Neuroimaging to Assess Structural and Functional Status of the Brains of Children and Adolescents Exposed to Drugs.**

Document the feasibility and accuracy of appropriate and acceptable methods for assessing brain structure and function of children and adolescents, with special attention to any or all of the following groups: those exposed to drugs during pregnancy, those passively exposed during infancy and childhood, and those actively using illicit substances. Documentation should include attention to such matters as technological difficulties and risks, and standardization issues relevant to testing conditions and image analysis.

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D. **Develop and Refine Methodologies for Drug Use Measurement Among Adolescents.**

Research to develop and refine methodologies for drug use detection and quantification, with special application to the adolescent with HIV infection or at high-risk for HIV infection. This research should address issues of acceptability, reliability, and validity of one or more methods (e.g., interviews, computerized questionnaires, and biological indicators such as saliva or sweat).

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E. **Develop and Test Reagents for the Diagnosis of Hepatitis C in Drug Users.**

Research to develop novel reagents such as virus particles, for use in community based testing for hepatitis C.

F. **Develop and Test Reagents for the Treatment of Liver Disease in Drug Users.**

Research to develop novel reagents either biological or chemotherapy based for treatment of liver disease in drug users. For example, reagent that modulation specific lipoproteins may reduce the progression of liver fibrosis.

G. **Develop a Diagnostic Test for Mitochondrial Dysfunction due to Illegal Drug Use.**

Research to develop a diagnostic test for mitochondrial dysfunction in Amphetamine/Methamphetamine users to determine tissue pathology, such as neurological disease.

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H. **Develop Methods/Batteries for Assessment of Vulnerability to and Emergence/Remission of Psychiatric Symptoms in Drug Abusers Under Treatment for Hepatitis C.** As drug abusers undergo Hepatitis C treatment symptoms of pre-existing mental disorders may re-emerge



and/or psychiatric symptoms may develop de novo. The context may include symptoms attributable to (1) significant pre-existing or emerging neuropsychological impairment, (2) drug intoxication/withdrawal, (3) active Hepatitis C and (4) co-morbidities associated with the above. This effort will develop reliable, valid, easily administrable test methods/batteries to promote the early detection and ease of ongoing assessment of these symptoms, including discrimination of symptoms attributable to each of the above in ways that effectively guide interventions in all of these areas.

- I. **Develop New or Improved Prescription Drug Adherence Assessment Measures and Procedures.** Develop measures and procedures to assess adherence to prescribed regimens for medications with significant abuse liability, e.g., opiates, benzodiazepines, sedative-hypnotics but which are extremely useful in the treatment of co-morbid psychiatric/medical conditions (such as depression, anxiety, dyssomnias, pain) in drug abusing populations. In this context there is concern about both the development of and relapse to patterns of abuse of these prescribed medications as well as continued use in accordance with medical instruction. Thus, this effort encourages the development of methods to monitor levels and patterns of use/abuse.

Methods may range from biological and physiological to psychological. Examples of biological methods include quantitative detection of the medication or a metabolite in body fluids and administration of a more easily detectable indicator substance in conjunction with the active medication. Physiological methods may include such efforts as monitoring of parameters related to heart rate, blood pressure, galvanic skin response and electroencephalographic measures. Psychological methods may include such efforts as automated cognitive or perceptual performance assessment and methods for systematic monitoring of administration patterns by significant others. Methods must be able to detect and quantify deviation from prescribed patterns of use in the directions of overuse or underuse in order to detect such phenomena as steady increases in amount used, sequestration of medications for binges or overdoses and diversion.

- J. **Develop Assessment Instruments to Detect Occult Drug Abuse in Clients/Patients Seen in the Mental Health, Medical Care, Social Service and Criminal Justice Systems.**

Develop diagnostic measures to be used by mental health, primary and specialty health care providers, and workers in the social service and legal systems to detect drug abuse in patients/clients whose drug abuse otherwise would remain undiagnosed. Such assessment instruments, could include (1) instruments based on structured or semi-structured interviews assessing such domains as symptom profiles, medical/psychiatric history, illness patterns consistent with drug abuse, (2) paper-and-pencil and/or computer-based questionnaires, surveys, or other testing modalities, (3) psychophysiological methods such as galvanic skin response, electroencephalography, eye movement/pupillometry testing, reaction time measures, heart rate/blood pressure responses, and functional brain imaging and/or (4) tests involving body fluids or other samples, such as gene activation patterns diagnostic of drug abuse. Portable, easily administered and highly sensitive and specific test batteries for drug abuse would be of great value in that they would (a) provide health care/social services providers with an awareness of a patient's otherwise undisclosed drug abuse -- which likely would have medical consequences in the form of drug interactions and other adverse effects related to the presence of drugs of abuse in patients undergoing treatment, receiving social services and/or having involvement in the criminal justice system and (b) provide a basis for the linkage of drug abuse treatment to the other interventions required.

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- K. **Development, Testing, and Dissemination of Innovative HIV/AIDS Prevention Intervention Technologies.**

1. Development and standardization (including assessment of psychometric properties) of self-report, physiological, and/or biological measures for use in HIV/AIDS prevention intervention in a variety of settings.

2. Development and validation of risk profiles and assessment methodologies for identification of individuals at-risk for HIV/AIDS.
3. Development and evaluation of HIV/AIDS prevention curricula, materials and implementation methods, for HIV/AIDS prevention service delivery.
4. Development of HIV/AIDS prevention intervention dissemination technologies, mechanisms, and links that integrate research with practice; specifically the transfer of HIV/AIDS prevention information to practitioners, policy makers, and the public.
5. Development of training modules for program implementers of research based HIV/AIDS prevention programs.
6. Development of strategies for the integration of proven HIV/AIDS prevention approaches into existing service delivery systems.
7. Development of innovative methodologies for data collection, data storage, data dissemination, and reporting techniques pertaining to HIV/AIDS prevention.

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#### **Other Research Topic(s) Within the Mission of the Institute**

NIDA encourages applications in other areas of research that may not be listed.

For additional information on research topics, contact:

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For administrative and business management questions, contact:

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#### **NATIONAL INSTITUTE ON DEAFNESS AND OTHER COMMUNICATION DISORDERS (NIDCD)**

The NIDCD supports research on the normal mechanisms of, as well as on diseases and disorders of hearing, balance, smell, taste, voice, speech and language. The Institute also supports research related to disease prevention and health promotion. The NIDCD addresses special biomedical and behavioral problems associated with people who have communication impairments or disorders. The NIDCD also supports efforts to create and refine devices, as well as develop cellular-based applications that may replace or substitute for lost and impaired sensory and communication functions. For more specific information about areas of interest to the NIDCD, please visit our home page at <http://www.nidcd.nih.gov/>.

#### **Hearing Program**

Research and development related to lost auditory function. Development of new cellular and tissue-based applications, hearing aids, cochlear implants, and other assistive devices (e.g., systems designed to improve access to and to increase utilization of computer and other information technologies, telecommunication devices, alerting systems) for individuals with hearing impairments; development of molecular technologies, including viral and non-viral vectors to enable gene transfer to the inner ear; development of cell type specific markers and probes to examine cell lineage in inner ear regeneration; development of research tools such as software and imaging technologies; development of relevant web or other databases; development of assays (including DNA-based assays), tests and instruments for the screening and diagnosis of hearing impairment, especially in neonates and infants; development of treatment modalities to prevent or lessen the effects of hearing disorders; development of new outcome measures for assessing the efficacy of treatments of hearing disorders; development of new research tools to aid in the study of the auditory system (e.g., imaging techniques, neuroanatomic tracers, electrophysiologic technology, new animal models); development of technologies for the study, diagnosis and treatment of otitis media including non-invasive

diagnostics to identify middle ear pathogens, novel antibacterial strategies, and prophylactic anti-microbial strategies.

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### **Balance/Vestibular Program**

Research to develop and refine tests of balance and vestibular function. Balance disorders affect a large proportion of the population, particularly the elderly. The vestibular system, with its receptor organs located in the inner ear, plays an important role in the maintenance of one's orientation in space, the control of balance while the body is immobile and in motion, and visual fixation of objects during head movement. Emphasis is on research and development of treatments for balance disorders; development of neuroimaging techniques and biochemical markers of disease in the vestibular system; development of systems to assess balance/vestibular function and for assessing the efficacy of physical rehabilitative regimens for balance disorders; development of a comprehensive software system to assess eye movements associated with the vestibulo-ocular reflex; development of instrumentation and a clinical test protocol for assessing the vestibulo-ocular reflex during locomotion; development of instruments and tests for assessing otolithic function; development of instruments and tests measuring head stability during natural stimulation of the vestibular system; development of perceptual reporting techniques and psychological indices for the clinical assessment of the balance-disordered patient; development of new outcome measures for assessing the efficacy of physical rehabilitative regimens for balance disorders; and development of assistive devices for balance disorders, including prostheses involving electrical stimulation of the vestibular system.

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### **Voice, Speech, and Language Programs**

Research on studies of voice, speech, and language disorders focuses on determining the nature, causes, treatment and prevention of disorders such

as stuttering, spasmodic dysphonia, dysarthria, and aphasia. Emphasis is on research and development of diagnostic measures and intervention strategies for voice, speech, swallowing, and language disorders; development of communication and other assistive devices for individuals with voice, speech, swallowing, and language disorders; identification and development of computer and animal models for research in communication disorders; development of new systems for visual communication by individuals who are deaf or severely hearing impaired; development of new systems of communication for individuals with motor impairment; design and development of diagnostic measures or materials for early identification of speech and language impairment in children; development of tests for the assessment of childhood and adult language impairment in multi-cultural populations; development of assessment measures of sign language abilities; development of improved artificial larynges and tracheoesophageal shunts; development of artificial intelligence computer models that simulate normal and disordered speech and language.

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### **Smell and Taste Program**

Research on the study of the chemical senses of taste and smell to enhance understanding of how individuals communicate with their environment. Improved understanding of the interaction between chemoreception, food consumption and diet will lead to improved nutrition from birth to old age. Both the olfactory and gustatory systems offer special approaches for understanding fundamental mechanisms of plasticity. Advances in molecular and cellular biology, biophysics, and biochemistry of the olfactory and gustatory systems are paving the way for improved diagnosis, prevention, and treatment of chemosensory disorders. Emphasis is on research and development of diagnostic tools for testing human smell and taste function; intervention strategies for smell and taste disorders; biosensors and electronic noses for industrial applications, and

other assistive devices for chemosensory impairments; innovative approaches for obtaining functional expression of mammalian odorant receptors in heterologous cells and for assessing ligand-receptor specificities; development of an inventory of chemicals at exceptional high purity for chemosensory research; development of a non-invasive drug delivery system using the primary olfactory nerve to target drugs or vaccines to the central nervous system; development of model systems using stem cell populations from the olfactory and taste sensory organs for the study of neurogenesis; development of readily administered chemosensory tests for population studies; and development of tests to differentiate trigeminal from olfactory and gustatory stimulation.

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#### **NATIONAL INSTITUTE OF DENTAL AND CRANIOFACIAL RESEARCH (NIDCR)**

The NIDCR conducts and fosters research on the etiology, pathogenesis, prevention, diagnosis, and treatment of oral, craniofacial and dental diseases and conditions. For more specific information about areas of interest to the NIDCR, please visit our home page at <http://www.nidcr.nih.gov>.

#### **Developmental Biology and Mammalian Genetics**

Emphasis is on the understanding of the development of tooth and bone, and on the identification of the genetic and environmental contributions to craniofacial disorders. The objective of this scientific program is to elucidate the underlying causes of craniofacial disorders, thereby advancing the fields of diagnosis, treatment, and prevention.

- A. Develop and operate registries to track craniofacial birth defects, diagnostic techniques, treatment protocols, and outcome assessments.
- B. Develop and manage tissue banks and/or DNA libraries of samples from patients with craniofacial birth defects and from unaffected relatives to aid in prospective and retrospective epidemiology and linkage studies to facilitate the discovery of genes involved in craniofacial dysmorphologies.
- C. Production of genetic and immunological markers specific for developing craniofacial tissues (e.g., stage specific markers for discrete populations of premigratory, migratory, and differentiating neural crest cells).
- D. Develop early pregnancy genetic tests to screen fetal cells in maternal blood for genetic mutations involved in inherited syndrome and non-syndrome craniofacial defects.
- E. Develop instrumentation to improve the diagnosis and treatment of inherited and acquired craniofacial defects.
- F. Develop instrumentation and methods to more accurately measure craniofacial growth in order to assess normal growth patterns as well as the effects of treatment procedures.
- G. Develop animal models possessing specific genetic craniofacial anomalies for use in studies on the etiology of disease, gene regulation, gene/environment analysis, and gene-product function and development of treatment protocols.
- H. Develop improved appliances to aid suckling by newborn infants with cleft palate and cleft lip.

#### **Infectious Diseases and Immunity**

Research relating to the etiology, pathogenesis, prevention, diagnosis and treatment of infectious diseases of the oral cavity is supported by the

NIDCR. This includes research on practical ways to effectively use the host immune system to prevent or treat oral infectious diseases and microbial-induced inflammation. Infectious diseases of the oral cavity include caries, periodontitis, candidiasis, peri-implantitis, pulpitis, and various viral and fungal infections of the oral mucosa and research on the diagnosis and prevention of oral manifestations of HIV infection and AIDS.

- A. Develop improved instrumentation, methodology, biomarkers or molecular probes for the rapid diagnosis and measurement of infectious diseases.
- B. Develop diagnostic tests to determine host susceptibility to oral infections.
- C. Develop ways to overcome or eliminate the risk of oral infections in persons who smoke or chew tobacco, drink alcohol, or are immunosuppressed, have diabetes, are malnourished, or are psychologically stressed.
- D. Explore novel methods or agents to eradicate oral biofilms (dental plaque) on teeth, oral soft tissues, and dental implants without adversely affecting the normal oral flora.
- E. Isolate, synthesize or prepare new antibiotics and antimicrobial agents that can overcome bacterial and fungal resistance to current compounds. Formulate combinatorial drug regimens to attack microbes growing in oral biofilms (dental plaque).
- F. Develop controlled release drug delivery systems for the prevention and control of oral infectious diseases.
- G. Develop biological response modifiers or other immunological approaches to reduce or eliminate microbial-induced chronic inflammation or the tissue destruction associated with chronic inflammation in the oral cavity.
- H. Provide methodologies to exploit the genome of oral bacterial pathogens.
- I. Develop improved animal or in vitro models of oral infectious diseases to enable evaluation of pathogenesis and therapies.
- J. Develop ways to interfere with microbial colonization and growth through the use of antimicrobial agents, chemotherapy or vaccines.
- K. Establish needed services that will benefit oral health care providers or research laboratories involved in the study or treatment of oral infectious diseases. Such services might be facilities for: software design; design and preparation of peptides and molecular probes; establishing and culturing hybridomas; determining antimicrobial sensitivity of microbes growing in biofilms (dental plaque) to drugs and antibiotics; or high technology imaging.
- L. Establish practical methods to increase host immune and non-immune defenses against infectious diseases (e.g., vaccines, biological response modifiers). Develop adjuvants to stimulate mucosal immunity. Identify and characterize target antigens for vaccines.
- M. Develop technologies for detecting and eradicating microbial biofilms in dental equipment.
- N. Develop methods for early diagnosis of oral opportunistic infections in asymptomatic individuals exposed to HIV.
- O. Develop diagnostic tests utilizing whole saliva and oral biopsies for examination of local immune responses and for the and assessment of disease progression
- P. Develop computer programs to model biologically active peptide regions of oral components that have anti-fungal, anti-bacterial and anti-viral activities.
- Q. Develop substitutes of naturally occurring chemicals (phytochemicals) known to have a role in controlling opportunistic infections induced by HIV.
- R. Develop synthetic peptides and recombinant proteins of oral components with anti-fungal, anti-bacterial and anti-viral, specifically HIV, activities.
- S. Develop controlled release delivery systems for local delivery of synthetic peptides recombinant proteins with anti-fungal, anti-bacterial and anti-HIV activities and of drugs.
- T. Develop and/or improve innovative and highly sensitive molecular techniques to examine changes of cytokines and other immune regulators, and of viral load in oral tissues and fluids.



## Epithelia Cell Regulation and Transformation

Emphasis is on the molecular mechanisms of oral epithelial cell regulation and aberrations of these mechanisms as they relate to the development and progression of diseases involving the oral mucosa including oral neoplasias research related to early diagnosis, prevention, and treatment of oral neoplasias.

- A. Develop immunological methods, imaging techniques or genetic markers for the early detection, diagnosis and prognosis of pre-malignant head and neck lesions including oral carcinomas.
- B. Develop methods for the rapid and specific detection of viruses implicated in the etiology of oral cancer as well as the detection of viral genes in pre-malignant and malignant head and neck lesions.
- C. Develop vaccines effective against viruses suspected to be etiologic agents in the induction of pre-malignant and malignant head and neck lesions.
- D. Develop novel techniques for the evaluation of chromosomal changes in head and neck cancers.
- E. Develop effective pharmacological, immunological and radiological modalities for treatment of pre-malignant and malignant head and neck lesions.
- F. Develop novel technologies for the genetic and molecular-targeted therapy of head and neck carcinomas.
- G. Develop animal models of localized and metastatic head and neck squamous cell carcinomas.
- H. Develop novel proteomic as well as micro and nano sensor technologies that can aid in early detection of head and neck tumors and can release therapeutic agents in tumor cells.
- I. Develop regimens for the alleviation of the oral complications of cancer therapy.
- J. Develop novel technologies for using stem cells as therapeutics for head and neck cancers.

## Physiology, Pharmacogenetics and Injury

Emphasis is on the normal and abnormal functions of the salivary gland, tooth and bone, physiology and cell biology of injury, trauma and wound healing, and

pharmacogenetics of drugs used in treatment of salivary as well as tooth and bone disorders.

- A. Develop viral and non-viral vectors for salivary gene therapy and gene therapeutics.
- B. Develop non-invasive methods for the determination of the efficacy and safety of artificial saliva, sialogogues and of their delivery vehicles.
- C. Develop recombinant proteins and synthetic-peptides of salivary molecules with known activities as well as vehicles for their delivery.
- D. Develop apparatus for craniofacial bone distraction that is contained entirely within the oral cavity.
- E. Develop more efficient methods, materials, and devices for prevention of injuries to the teeth, mouth, and face during athletic activities.
- F. Develop diagnostic reagents and tests necessary to effectively use changes in saliva to diagnose and monitor specific disease processes, drug therapy, genetic defects, nutritional status, and age-specific therapy.
- G. Develop and characterize immortalized normal human and rodent salivary gland epithelial cell lines with appropriate phenotypic expression.
- H. Develop artificial saliva and/or drugs (sialogogues) for the treatment of xerostomia and develop controlled release delivery systems for their delivery at desired sites.

## Molecular and Cellular Neurobiology

Emphasis is on research on chronic disabling diseases of the oral-craniofacial-dental areas including neuropathies and neurodegenerative disorders, diseases of the temporomandibular joint.

- A. Develop improved technics for measuring chemosensory, tactile, kinesthetic, or proprioceptive function involving craniofacial structures. Such measures may be useful in screening for deficits, improving diagnosis, or for evaluating responses to dental treatments or interventions.
- B. Develop improved measures for assessing oral-motor coordination or oral behaviors (e.g., swallowing, masticatory efficiency).
- C. Develop improved biomarkers or treatments for neuropathic conditions or neurodegenerative



conditions affecting oral-craniofacial tissues or structures.

- D. Develop assays facilitating reliable evaluations of relationships between hormonal or chronobiological variations and other risk factors as these relate to onset or exacerbation of pain symptoms.
- E. Develop improved in vitro or animal models for evaluating biomechanical, wear, functional or systemic responses associated with TMJ devices or engineered tissues.
- F. Develop improved in vitro or animal models for assessing pathobiological changes in the TMJ or masticatory muscles and improved biochemical markers of joint degradation.
- G. Develop innovative approaches to reduce foreign body reactions or to improve surgical outcomes for prosthetic devices or bone grafts received subsequent to failed alloplastic TMJ implants
- H. Develop safe and effective biomaterials or procedures useful in repairing the temporomandibular joint (TMJ) following trauma, degenerative or inflammatory diseases processes, or iatrogenically-induced pathology (e.g., failed TMJ implants).
- I. Develop more efficient methods, materials, and appliances for orthodontic tooth movement.
- J. Develop improved appliances to aid suckling by newborn infants with cleft palate and cleft lip.

### Biotechnology and Biomaterials

Emphasis is on the development of natural and synthetic materials to be used for the repair, regeneration, restoration and reconstruction of oral tissues and organs; on the development and improvement of evaluation and measurement systems for the characterization of implanted material properties; on their interactions as well as on their performance under the conditions of the biological environment; and finally on the development and/or improvement of new dental restorative materials that are mercury free.

- A. Develop strategies for the fabrication of site-specific repair and regeneration systems (e.g., smart implants to specifically attach the appropriate reparative cells).
- B. Establish libraries of structural recognition epitopes (peptides, carbohydrates) to screen

biological activities (e.g., bacterial adherence to soft and hard oral tissues).

- C. Develop non-destructive methods for the characterization of material properties in vivo and in vitro.
- D. Develop synthetic analogues of oral/craniofacial tissues and organs.
- E. Develop more sensitive methods to determine and measure the interactions of materials with biological systems (e.g., material biocompatibility and bioactivity in the oral environment).
- F. Optimize imaging techniques for describing the architecture of oral tissues and structures.
- G. Develop computer and mathematical modeling systems capable of mimicking biological tissues and of evaluating material designs.
- H. Develop novel techniques for ensuring sterility of biomimetic structures prior to implantation.
- I. Develop delivery systems that are compatible with host immunity; consider hybrids and artificial vectors as well as viral and non-viral gene delivery systems with cell-type selectivity.
- J. Develop in vitro methods that predict immunogenicity to vectors used for gene transfer as well as for biomaterials.
- K. Develop improved implantable materials, designs through nanotechnology principles.
- L. Develop improved surgical techniques for artificial implants to support replacement of dental, oral and craniofacial tissues and organs.
- M. Develop new and improved instruments and techniques for the diagnosis and treatment of TMDs.
- N. Develop improved composite materials and adhesive sealants suitable for restoring crowns of posterior teeth and exposed roots of teeth.
- O. Utilize nanoscience and nanotechnology principles in the development of new non-mercury containing dental restorative materials.
- P. Design and development of orthodontic and other prosthetic appliances.

## Clinical, Epidemiological, and Behavioral Research

Provides support for clinical trials and patient-oriented research on the safety, efficacy, and effectiveness of measures for diagnosing, preventing, or treating oral, dental, and craniofacial conditions and disorders, as well as for research on the distribution of such disorders, risk and protective factors, oral health disparities, and basic and applied behavioral, social science and health services research relevant to oral diseases and their prevention or treatment.

- A. Develop and test web-based training or other innovative approaches to accelerate accurate translation of new knowledge regarding oral diseases and their effective prevention/treatment into clinical or public health practice.
- B. Conduct studies to expand knowledge regarding specific oral health consequences of using various smoked or smokeless tobacco products.
- C. Develop reliable, sensitive, cost-effective measures for improved assessment of oral health status in populations or population subgroups.
- D. Develop and test tobacco prevention and cessation programs involving dental settings or oral health markers.
- E. Develop and test the effectiveness of innovative teaching tools to inform oral health professionals or the public regarding oral cancer prevention and early detection.
- F. Develop and test devices or methods to improved time-sampled monitoring of behavioral adherence with preventive or therapeutic regimens specifically relevant to oral diseases/conditions. Such devices or methods could be utilized either within clinical trials or oral health care delivery processes and systems.

## Other Research Topic(s) Within the Mission of the Institute

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## NATIONAL INSTITUTE OF DIABETES AND DIGESTIVE AND KIDNEY DISEASES (NIDDK)

The NIDDK supports research in diabetes, endocrinology and metabolic diseases; digestive diseases and nutrition; and kidney, urologic and hematologic diseases. For additional information about areas of interest to the NIDDK, please visit our home page at <http://www.niddk.nih.gov>.

## Diabetes, Endocrinology and Metabolic Diseases

The Division of Diabetes, Endocrinology and Metabolic Diseases supports basic and clinical research on the etiology, pathogenesis, prevention, diagnosis, and treatment of diabetes mellitus and its complications; endocrine diseases; osteoporosis; cystic fibrosis, and other metabolic disorders; as well as research on basic endocrine and metabolic processes. Research topics of potential interest to small businesses include, but are not limited to:

### DIABETES

- A. Development of non-invasive, minimally invasive or implantable sensors for monitoring blood or interstitial fluid glucose and/or integration of glucose sensor and insulin

delivery systems to create an artificial pancreas.

- B. Development of improved insulin delivery methods or devices.
- C. Development of techniques or products useful for predicting, preventing or delaying progression of diabetes, including tests for identifying patients at risk, methods of monitoring progression.
- D. Development of immunomodulation/ tolerance induction strategies to prevent type 1 diabetes.
- E. Development of strategies or tools to support the application of behavioral approaches to risk reduction in the development of type 2 diabetes or to the improved treatment of diabetes. An important consideration should be cost and practicability of use.
- F. Development of products, such as animal models or surrogate markers for identification of disease progression, useful in evaluating potential therapies for diabetes and its complications.
- G. Development of new therapies to prevent or delay complications of diabetes.

#### ISLET TRANSPLANTATION

- A. Development of antibodies to cell surface markers on mammalian stem/progenitor cells that can be converted into islet like cells so as to facilitate prospective cellular identification and purification.
- B. Development of methods that protect islet grafts after transplantation and minimize the use of immunosuppression through immunomodulation/tolerance induction or immunoisolation.
- C. Development of methods to increase the yield and reproducibility of functional and successfully transplantable islets from human pancreata including the use of recombinant enzymes as a replacement for the mixture of purified naturally occurring enzymes currently used.
- D. Development of methods that expand the number of human islets during culture while still retaining appropriate functional islet characteristics and the ability to be successfully transplanted.
- E. Development of pre-transplant islet testing approaches that are predictive of subsequent

successful islet transplantation using functional genomics, proteomics or other methods.

- F. Development of non-invasive imaging methods for the *in vivo* measurement of pancreatic beta cell mass, function or inflammation after transplantation of pancreatic islet/beta cells.
- G. Development of methods utilizing replenishable cell sources, especially stem cells, that produce functional islet like cells/tissues that can be successfully transplanted.
- H. Development of methods for increasing the duration for which a human pancreas can yield functional and successfully transplantable islets.
- I. Development of methods to improve viability/function of islets prior to transplantation and the engraftment and long term function of islets after transplantation.

#### CYSTIC FIBROSIS

- A. Development or improvement in diagnostic or screening tests for cystic fibrosis.
- B. Development of potential therapeutics for CF including agents to improve trafficking and function of mutant CFTR, to enhance activities of channels which can serve as alternatives to CFTR, and to increase transcription or translation of CFTR RNA.
- C. Development of products useful in assessing or improving nutritional status in patients with CF including improved pancreatic enzyme preparations.
- D. Development of approaches to gene transfer for cystic fibrosis by improving gene delivery systems, improving tropism for target cells, increasing efficiency and duration of transgene expression and minimizing toxic effects.

#### GENETIC METABOLIC DISEASES

- A. Development of improved methods for the diagnostic, population or newborn screening or prenatal testing for genetic metabolic diseases.
- B. Production of stabilized biologically active proteins or peptides useful for enzyme replacement therapy.
- C. Improvements in the construction of gene therapy vectors to increase transduction efficiency, level and duration of expression, and to improve targeting.

- D. Development of improved methods of manufacturing gene therapy vectors that are scalable and improve titer and bioactivity of the vectors.
- E. Development of new vector systems that improve the ability to transduce nondividing cells such as hematopoietic stem cells, neurons, hepatocytes or epithelial cells.
- F. Development of techniques to achieve efficient homologous integration or site-specific integration of introduced genes.

#### **METABOLIC PROFILING**

- A. The development of novel metabolomics technologies (large-scale approaches for metabolic profiling) to study diabetes or other endocrine or metabolic diseases.
- B. Development of improved methods for monitoring metabolic control in diabetes.

#### **HORMONE ACTION**

- A. Identification of new ligands for previously unclassified (orphan) nuclear receptors.
- B. Development of partial agonists or antagonists with therapeutic potential in diseases such as diabetes and osteoporosis, hormone-dependent cancers, and for conditions such as obesity.
- C. Development of Selective Receptor Modulators (SRMs) with tissue specificity and profiles that provide beneficial effects without side effects obtained from therapies based on naturally occurring hormones.

#### **APPLICATION OF PROTEOMICS TO DIABETES AND OTHER ENDOCRINE AND METABOLIC DISEASES**

- A. Identification of surrogate markers looking at the plasma/sera proteome at different stages of diabetes or other endocrine or metabolic diseases.
- B. Development and/or use of computational proteomics tools to analyze and/or annotate the genome as it might apply to information relevant to diabetes or other endocrine or metabolic diseases.
- C. Development of novel proteomic technologies designed to understand the physiology or improve the diagnosis of diabetes or other endocrine or metabolic diseases.

- D. Identification of novel drug targets or novel therapeutic agents using proteomic approaches that might be relevant to diabetes or other endocrine or metabolic diseases.
- E. Characterization of the proteome or a subset of the proteome for toxicology studies of drugs that might be relevant to diabetes or other endocrine or metabolic diseases.

#### **Digestive Diseases and Nutrition**

The Division of Digestive Diseases and Nutrition supports research on the function, diseases and disorders of the digestive tract; the esophagus, stomach, intestine, colon, anorectum, pancreas, liver, gallbladder, and biliary tract; basic, clinical and behavioral research on nutrition and obesity as well as information transfer in the field of digestive diseases and prevention of obesity. Innovative investigator-initiated projects that are not mentioned below are encouraged. Areas that may be of interest to small businesses include, but are not limited to:

#### **DIGESTIVE AND LIVER DISEASES (CLINICAL)**

- A. Development of assays to detect biomarkers for genetic predisposition to GI-relevant diseases, e.g., IBD and IBS.
- B. Development of new genetic screening methods for detection of inherited digestive and nutritional disorders, e.g., hemochromatosis, Wilson's disease, Crigler-Najjar syndrome, Alagille syndrome.
- C. Development of improved means for detecting Barrett's esophagus.
- D. Development of a non-invasive means of localizing GI bleeding beyond the duodenum that is more sensitive than the Tc-RBC test.
- E. Development of methods for gastrointestinal endoscopy without the need for sedation.
- F. Development, using rationale drug design techniques, of agents that interact with L-type calcium channels or with delayed rectifying potassium channels to treat motility disorders (pseudo-obstructive disorder, chronic constipation, and slow bowel transit).
- G. Development and validation of herbal, ayurvedic, Chinese traditional, Kampo or other treatments for common GI ailments and liver diseases such as motility disorders, IBD, and cirrhosis.

- H. Development of pharmaceuticals from herbal preparations of promise for therapy of digestive diseases, including liver diseases, involving isolation of active components, preparation of pharmacologically pure preparations, and testing for pharmacokinetics and activity in humans.
- I. Development of novel antifibrotic therapies for progressive liver failure.
- J. Development of agents that would protect the gut epithelium from the damage caused by chemotherapeutic agents.
- K. Development of tests of hepatic "reserve" which would be of use, for example, in assessing the risk of surgery in patients with liver disease.
- L. Development of agents to promote the repair of gut epithelium barrier function, e.g., as needed following chemotherapy.
- M. Development of drugs for dissolving gallstones in vivo.
- N. Development of humanized monoclonal antibodies against HCV and HBV to be used for prevention of recurrent disease in liver transplant patients.
- O. Development of surrogate markers for liver fibrosis and progression.
- P. Development of a rapid, non-invasive diagnostic test for biliary atresia.

#### **DIGESTIVE AND LIVER DISEASES (BASIC)**

- A. Development of detection methods for non-culturable forms of gut enteric bacteria.
- B. Development of molecular probes for the diagnosis of mucosal dysplasia in inflammatory bowel disease.
- C. Development of new techniques, including non-invasive imaging, to measure motility/intestinal transit at various sites within the gastrointestinal tract.
- D. Development of techniques for the preservation and transplantation of small intestine and pancreas.
- E. Development of non-invasive measures of pancreatic exocrine function.
- F. Development of a test for determining the hepatotoxic potential of drugs, agents or additives that is more sensitive than testing in

mice and reflects the human response to the test compound.

- G. Development of animal models to study hepatotoxic agents.
- H. Improvements to existing imaging systems, or development of new ones, to allow non-invasive detection of fibrotic, necrotic, inflamed, and fatty livers prior to transplantation.
- I. Development of non-invasive techniques to detect liver disease.
- J. Development of non-invasive imaging methods to assess fatty liver in patients.
- K. Development of non-invasive devices/techniques to measure portal pressure for evaluating portal hypertension in patients with cirrhosis.
- L. Development of an extracorporeal liver assist device to provide temporary therapeutic assistance in cases such as fulminant hepatic failure or drug overdose.
- M. Development of non-occluding stents for use in the biliary tract and in transjugular intra-hepatic porto-systemic shunts (TIPS).
- N. Development of cryopreservation techniques for human hepatocytes that would maximize viability and cell culture growth potential of thawed cells.
- O. Creation of artificial organs or development of effective xenographic techniques for liver transplantation.
- P. Development of molecular standards for Hepatitis C virus quantitation and typing.
- Q. Development of molecular standards for Hepatitis B virus quantitation and typing.

#### **NUTRITION**

- A. Development of a better method for measuring food intake patterns of individuals that could replace recall.
- B. Development of better methods for assessing overall nutritional status.
- C. Development of a non-invasive breath or blood test to accurately measure dietary fat intake.
- D. Development of biological measures, such as serum or urine tests, for long-term dietary consumption of specific nutrients.



- E. Development of better means of assessing energy intake and/or energy expenditure (i.e., physical activity), e.g., a device to estimate movement and relate this to calories expended with the goal of impacting behavior and preventing obesity.
- F. Development of better means to detect food borne pathogens with the goals of (1) preventing their inclusion in foodstuffs and (2) better treatment of acute infections.

#### **OBESITY AND EATING DISORDERS**

- A. Development of sage drugs or herbal products that inhibit appetite or increase energy expenditure.
- B. Development of computerized interventions for weight-loss/maintenance and/or increasing physical activity such as hand-held computers and web-based programs.
- C. Development of devices/equipment/ interventions to encourage "activity" while performing sedentary work.
- D. New technologies for quantitative assessment of intra-abdominal fat; emphasis on technologies that are non-invasive, minimize the use of ionizing radiation, and have the capability of being adapted for use in the usual health care settings.
- E. Development of more economical methods to produce <sup>18</sup>O-labelled oxygen for use in energy expenditure studies and/or body composition studies using doubly labeled water.

#### **Kidney, Urologic and Hematologic Diseases**

The Division of Kidney, Urologic, and Hematologic Diseases supports research into basic mechanisms of organ and tissue function and into the diseases of the kidney, urologic and hematologic systems. Projects to help develop an understanding of the physiology, pathophysiology, and related diseases of the kidney, urinary tract, and blood and blood forming systems so that rational treatments and means of prevention and/or arrest of diseases may be devised. Support for advances in the technology of cell and molecular biology that will enhance research in kidney, urologic and hematologic diseases is encouraged. Research opportunities of interest to small businesses include, but are not limited to:

- A. Development of a genomic toolbox for study of kidney, prostate, bladder, or red cells, which would include:
  1. Library generation and gene identification from whole organ or rare compartments in normal, developing, or injured tissues.
  2. Antibodies or phage libraries that will facilitate the prospective identification and purification of renal cell types.
  3. Strategies to deal with the anatomical complexity, increase the representation of low abundance transcripts, or decrease the redundant sequencing of over-represented or known genes.
  4. Bioinformatic tools.
  5. Flexible databases useful for designing organ-specific databases and websites.
  6. Techniques for visualizing RNA distribution within cells or tissues.
  7. New methods to acquire material from archival samples.

#### **KIDNEY**

- A. Development of monoclonal antibodies specific for the individual cell types of the renal glomerulus, proximal and distal tubules, loops of Henle, and collecting ducts.
- B. Development of both data and cell banks of diabetic kidney disease families for use by the research community.
- C. Development of pharmacological agents that might be used to intervene in inflammatory renal disorders and in disorders of renal hemodynamics, blood pressure, and extracellular volume regulation.
- D. Means to achieve a more stable physiologic homeostasis in maintenance dialysis therapy to overcome the physiologic consequences of intermittent hemodialysis through the:
  1. Improvement of blood access to permit continuous access to the circulation.
  2. Development of means to provide for continuous anticoagulation.
  3. Development of reliable, non-invasive, on-line hemodialysis monitoring systems assessing real-time treatment parameters such as blood volume, access flow, and urea clearance.

- E. Studies to improve the efficiency of maintenance dialysis:
  - 1. Development of innovative methods to produce more efficient and less morbid forms of renal dialysis (e.g., GI dialysis, artificial kidney).
  - 2. Studies on biocompatibility of artificial kidney membranes, in surface sensitive proteins, complement, and clotting mechanisms.
  - 3. Development of new agents for sterilizing dialysis membranes.
  - 4. Development of new dialysis membranes to diminish the duration of dialysis treatments.
- F. Improved techniques of preservation and storage of kidneys intended for transplantation.
- G. Development of material(s) for construction of urinary catheters that may reduce the incidence of infection in the urinary tract.
- H. Development of both data and cell banks of autosomal and recessive polycystic disease families for use by the research community.
- I. Development of improved renal imaging techniques, differential renal function assessments and diagnostic distinction between benign and malignant parenchymal diseases.
- J. Development of new therapies for rare diseases of the kidney and urinary tract.
- K. Computer-Assisted Diagnosis and Teaching in Acid-Base and Electrolyte Disorders.
- L. Development of methods to provide early diagnostic tools, preventative measures, and treatment modalities for Acute Renal Failure.
- M. Identification of mediators of renal failure during sepsis and pharmacological means to block these effects.
- N. Development of new non-invasive methods for measuring kidney function:
  - 1. Reliable, non-invasive, non-radioactive methods of measuring glomerular filtration rate (GFR).
  - 2. Identification and description of physiologic compounds that are filtered by the kidney, but neither secreted or reabsorbed;
  - 3. Identification of serum factors released by damaged kidney cells.
- 4. Characterization of changes in kidney hormonal function in kidney disease at various stages of severity.
- 5. Development of new markers of early kidney dysfunction.
- 6. Development of markers that are predictive of end stage renal disease.
- 7. Development of rapid, accurate, and cost effective means of quantifying urine albumin.
- O. Development of sensitive techniques to identify open reading frames of chromosomes in specialized tissues, such as the prostate or renal glomerulus; e.g., methods for developing a cDNA library with mRNA as a starting material.

#### UROLOGY

- A. Study of the effect of growth factors, hormonal concentrations and other biochemical stimuli on the growth of prostatic tissue. Analyses of factors responsible for initiation and progression of Benign Prostatic Hyperplasia (BPH).
- B. Development of animal or in-vitro models for the study of stromal - epithelial interactions in BPH.
- C. Assessment of factors responsible for Benign Prostatic Hyperplasia (BPH) induced uropathy.
- D. Host-parasite and bacteria-urothelial cell interactions involved in urinary tract infection.
- E. Kinetics of renal stone formation, such as characterization of growth and dissolution, or crystal growth inhibition, and definition of reliable biochemical profiles of stone forming patients.
- F. Development of additional therapeutic agents for prevention and/or treatment of urolithiasis.
- G. Neuropharmacological-neurophysiological assessments in urodynamics.
- H. Development of culture conditions for in vitro culture of cells from benign prostatic hyperplasia.
- I. Development of serum or urine markers that correlate with prostate size to evaluate rate of growth.

- J. Development of non-invasive instrumentation that can detect early onset of bladder instability associated with diabetes mellitus.

#### HEMATOLOGY

- A. Development of methods and equipment for routine high volume isolation of highly purified hematopoietic stem and progenitor populations.
- B. Identification of new methods to assay hematopoietic stem and progenitor cells with short- and long- term repopulation models amenable to serial examination.
- C. Development of chemically defined reagents that support hematopoietic stem cell proliferation and differentiation
- D. Definition of culture conditions using serum-free medium that will support the ex vivo expansion of hematopoietic stem and progenitor cells.
- E. Development of new approaches for identifying, isolating, and genetically analyzing fetal erythrocytes in the maternal circulation.
- F. Development of novel methods for the delivery of DNA, proteins, and other compounds to hematopoietic stem cells.
- G. Development of rapid, high throughput microarrays for accurate assessment of gene expression profiles of hematopoietic stem cells.
- H. Development of non-invasive systems for monitoring the total hemoglobin and hematocrit, suitable for use with adults or neonates.
- I. Application of nanotechnology to the measurement of blood parameters and diagnosis of blood disorders.
- J. Development of new methods for the non-invasive or minimally invasive measurement of body iron
- K. Adaptation of MRI technology for the non-invasive measurement of body iron:
1. Develop appropriate MR measurement method(s).
  2. Optimize RF coils for the body region of interest (primarily heart, liver, and pancreas).
  3. Develop magnets of the appropriate magnetic field strength(s).
  4. Develop a reliable method for calibrating and validating iron concentration detected by magnetic resonance imaging.

5. Determine the most appropriate magnetic resonance method for determining relaxation times and susceptibility.
6. Develop indicator materials for direct MR measurement of iron concentration.

- L. Design of therapeutic drugs for inducing fetal hemoglobin synthesis.

#### Other Research Topic(s) Within the Mission of the Institute

For additional information on research topics, contact:

#### DIABETES, ENDOCRINOLOGY AND METABOLIC DISEASES

##### Islet Transplantation

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##### Diabetes Therapy and Prevention

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##### Gene Therapy, Metabolic Diseases, and Cystic Fibrosis

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##### Proteomics, Glucose Sensors, Metabolic Profiling, and Hormone Action

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#### DIGESTIVE DISEASES AND NUTRITION

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### **KIDNEY, UROLOGIC AND HEMATOLOGIC DISEASES**

#### Kidney

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### **NATIONAL INSTITUTE OF ENVIRONMENTAL HEALTH SCIENCES (NIEHS)**

Human health and human disease result from three  
interactive elements: environmental exposures,

genetic susceptibility and age. The mission of the NIEHS is to reduce the burden of human illness and dysfunction from environmental causes by understanding each of these components and how they interrelate. NIEHS achieves its mission through a multidisciplinary biomedical research program, prevention and intervention efforts, and a communication strategy that encompasses training, education, and technology transfer and community outreach. NIEHS supports research and training focused on the identification, assessment and mechanism of action of agents in the environment that are potentially harmful to human health. The ultimate goal of these NIEHS activities is to then transfer this knowledge for the public benefit. The SBIR program uses a combination of research, technology transfer and communication strategies to aid the mission of NIEHS.

For additional information about the areas of interest to NIEHS, visit our home page at  
<http://www.niehs.nih.gov>.

### **Predictive Test Systems for Safety Evaluation Program**

NIEHS is interested in developing, standardizing, and validating sensitive and specific new and novel tests or batteries of tests that will provide faster and cheaper alternatives to the use of standard rodent toxicity tests, i.e., assays for carcinogenicity, immunotoxicity, reproductive or developmental toxicity, dermal toxicity, neuro or other organ system toxicity including general toxicity. The proposed tests should use cell cultures or animal models that can be extrapolated to human risk. Examples include but are not limited to:

- A. Develop animal stem cell models that can be used to test for toxicity on differentiation or differentiated function.
- B. Establish cell lines of differentiated human cells (e.g., derived from tissue stem cells) that are equivalent to in vivo tissues (i.e., models that maintain differentiated functions that are important for the toxicological phenomena under study) and develop in vitro endpoints that are extrapolatable to the in vivo biomarkers of toxicity.
- C. Develop biokinetic models that include the integration of toxicodynamic and biokinetic modeling to predict systemic toxicity.
- D. Develop and validate non-mammalian or invertebrate models for specific toxicities that

utilize endpoint that are conserved across species so the results can be extrapolated to human risk.

- E. Develop a battery of receptor binding (or activity) assays that will define agents that act via receptors and therefore will have growth factor, cytokine, endocrine or neurotransmitter activity.
- F. Development and prevalidation of assays to assess the ability of chemicals to pass through barriers (i.e., blood brain, kidney, lung, gastrointestinal).
- G. Model mechanisms of multicellular interactions in the development of toxic responses.
- H. Development and prevalidation of in vitro cultures to assess metabolism of toxicants, the enzymes involved and the nature of the metabolites formed.
- I. Development and prevalidation of assays to determine dermal irritation, dermal absorption, dermal hypersensitivity and phototoxicity.
- J. The endpoints for these assays should take advantage of the new technologies such as genomics, transcriptomics, proteomics, bioinformatics to develop high throughput systems for in vitro tests and novel endpoints (biomarkers) including non-invasive endpoints including reporter assays and the use of in situ fluorescence for in vivo systems.

### Exposure Assessment Program

NIEHS is interested in developing and validating new approaches, products/devices, tools, methods, biomolecules and biomaterials to improve our ability to measure exposure to environmental hazards. It is anticipated that bioengineering and nanotechnology will be used to provide the novel, sensitive, high throughput, miniaturized systems that are needed to improve our ability to measure both exposure to an environmental agent and its effects on the biology of the organism. Examples include but are not limited to:

- A. Use of genomics, proteomics and metabonomics to provide molecular fingerprints of exposure to environmental agents.
- B. Development of new, sensitive biomarkers of specific tissue damage that can be measured in serum, urine, or saliva.
- C. Personal multiplexed monitors to measure current or cumulative exposures to

environmental agents, both long lasting lipophilic and short-lived non-accumulating toxicants.

- D. Miniaturized sampling instruments for use with children.
- E. Development and validation of physiological biomarkers or surrogate markers of previous exposures to environmental agents.
- F. Nanotechniques to detect and assay environmental agents and their metabolites.
- G. Identification of toxic products/metabolites in blood, urine or saliva that could be used for screening large populations for exposure.
- H. Total exposure profiles for individuals that consider multiple sources (air, food, water) and multiple sites (residential, occupational, general environmental).
- I. High throughput fingerprinting of genetic polymorphisms for use in large-scale human studies.
- J. Development of sensor technologies for detection and analysis of biologically relevant molecular and physical targets of environmental agents in samples from blood, saliva and other body fluids.

### Hazardous Waste Assessment, Evaluation and Remediation Program

NIEHS is interested in developing biotechnology and bioengineering approaches for the development of novel strategies for assessing and evaluating exposure to hazardous waste and for reducing exposure via remediation technologies. Focus should be on the development of products or instruments to improve remediation including bioremediation and phytoremediation strategies as well as physical /chemical methods. In addition there is interest in developing products to improve monitoring of the extent and amount of contaminants as well as to monitor the effectiveness of remediation technology in both the short and long term. Examples include but are not limited to:

- A. Development of biostatistical software applications to interpret complex and diverse data sets investigating gene-environment, gene-gene, or multigene-environment interactions.
- B. Development of nano structures, electrochemical methods, photocatalytic



- processes, thermal treatments or filtration-based methods of remediation.
- C. Phytoremediation technologies using genetically engineered plants.
  - D. Development of bioremediation technologies using genetically engineered microbes and/or bioreactors.
  - F. Development of biosensors and field ready instruments to measure chemical contaminants.
  - G. Remediation methods specific to metals and metal-organic mixtures.
  - H. Development of technologies to monitor the bioavailability of remediation products or the change in bioavailability as a result of remediation.
  - I. Development of methods/instruments to detect and measure non-aqueous phase liquids and dense non-aqueous phase liquids in the subsurface.
  - J. Development of products to delineate subsurface geological structures and hydro-geological configurations and to sample for the presence of contaminants in these structures.
  - K. Development and validation of new biomarkers of exposure, effect and susceptibility especially for non-cancer endpoints.
  - L. Development of innovative monitoring technologies capable of measuring acute or long-term exposures to contaminants at environmental concentrations.

### Animal Model Program

NIEHS is interested in developing animal models that mimic human diseases that would be useful in showing direct links between exposures to environmental agents and the initiation or progression of the disease state. Models may also show gene-environment interactions in the initiation or progression of diseases. These models can be mammalian, non-mammalian, invertebrate or organ and cell tissues in origin. Genetically modified animals including those with reporter genes or in situ fluorescence or other non-invasive endpoints are also of interest. Animal models of particular interest include but are not limited to:

- A. Parkinson and other neurodegenerative diseases.
- B. Autoimmune and other immunologic diseases.

- C. Endocrine related diseases.
- D. Cardiovascular/gastrointestinal/liver/kidney diseases.

### Educational Material Program

NIEHS is particularly interested in developing educational materials related to teaching students of all ages and the lay community about environmental health sciences. These materials are an important part of our communication strategy that encompasses training, education, and community outreach. Educational materials may thus be directed at all ages from K-12 through adult education and community outreach. They may also be interactive programs/games, videos or databases. Educational materials on subjects such as risk assessment, hazards in our environment, use of pesticides, endocrine disruptors, air/soil/water quality and intervention/prevention strategies are of particular interest.

### Other Topics Within the Mission of the Institute

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### NATIONAL EYE INSTITUTE (NEI)

The NEI supports research with respect to blinding eye diseases, visual disorders, mechanisms of normal visual function, preservation of sight, and the special health problems and requirements of individuals with impaired vision. Proposals for all areas in basic and clinical vision research are encouraged. Some examples are listed below.

The NEI's programs are described in extensive detail in documents which are available from the Institute. For additional information about the research programs of the NEI, please visit our home page at <http://www.nei.nih.gov>.

### **Retinal Diseases Program**

Research and development of new therapeutic approaches for ocular inflammatory diseases and to inhibit abnormal proliferation of the retinal and choroidal blood vessels; development of better methods of diagnosing and treating diabetic retinopathy and other vascular diseases of the retina and choroid; development of non-invasive techniques for early diagnosis of macular degeneration and other retinal degenerative diseases; development of instruments and procedures for improved surgical management of retinal detachments.

### **Corneal Diseases Program**

Research and development of new therapeutic agents for the treatment of corneal diseases; development of innovative methods of drug delivery for ocular surface disorders; development of new biomaterials for corneal prostheses; development of instruments and procedures for correcting the refractive power of the cornea and measuring the cornea's optical and physiological properties.

### **Lens and Cataract Program**

Research and development of therapeutic agents for the prevention of cataract; development of new approaches in the post-operative management of cataract surgery; development of new surgical instruments for cataract extraction and biomaterials for replacement of the natural lens.

### **Glaucoma Program**

Research and development of new therapeutic agents, instruments, and procedures for the diagnosis and treatment of glaucoma; development of non-invasive methods to measure changes in the optic nerve head and retinal fiber layer.

### **Strabismus, Amblyopia, and Visual Processing Program**

Research into the identification and characterization of growth factors which facilitate regeneration of visual nerve axons; development of innovative techniques to study factors that facilitate

regeneration and guidance of developing or regenerating nerve fibers; development of new approaches using imaging techniques, such as PET and MRI, to localize lesions and test the functioning of specific parts of the visual system, especially those involved in higher order visual processing and oculomotor processing.

### **Visual Impairment and Its Rehabilitation Program**

Research and development of instruments and methods to better specify, measure, and categorize residual visual function; development and evaluation of optical, electronic, and other devices that meet the rehabilitative needs of persons who are blind or have low vision.

### **Other Research Topic(s) Within the Mission of the Institute**

For additional information on research topics, contact:

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### **NATIONAL INSTITUTE OF GENERAL MEDICAL SCIENCES (NIGMS)**

The NIGMS supports research and research training in the basic medical sciences and related natural and behavioral sciences and in specific clinical areas (i.e., clinical pharmacology, trauma and burn injury, and anesthesiology). The NIGMS also supports health-related research that is otherwise not assigned to another of the PHS components.

For additional information about areas of interest to the NIGMS, please visit our home page at <http://www.nigms.nih.gov>. This site includes staff contact information by program area ([http://www.nigms.nih.gov/nigms\\_staff/contact.html](http://www.nigms.nih.gov/nigms_staff/contact.html)). It also includes links to program announcements that highlight NIGMS areas of special emphasis (<http://www.nigms.nih.gov/funding/funding.html>). In some cases, these announcements specifically

mention the SBIR and STTR grant mechanisms, in most cases they do not. However, it is clear that small businesses could make contributions to the research objectives described in these announcements.

### Division of Cell Biology and Biophysics

Research on membrane synthesis, structure, and function; membrane models; membrane transport; cell division; cell organization; cell motility; and biophysics of proteins, nucleic acids, and biological assemblies, as well as the development of instrumentation, components, and methods for the analysis of cellular components and macromolecules by imaging, spectroscopy, and diffraction analysis.

SBIR and STTR proposals on the application of cell biology, biophysics, biochemistry, physics, mathematics, and chemistry to biomedical problems, and the development of instrumentation to facilitate research in cell biology and biophysics, such as, but not limited to, the topics listed below are welcome.

- A. Development and improvement of methods for the expression, solubilization, and purification of milligram quantities of regulatory, cellular, and membrane associated proteins, as well as for the preparation of specifically labeled macromolecules and the recovery of proteins from inclusion bodies.
- B. Development of novel ligands, inhibitors, and other probes for spectroscopic and microscopic analysis of cellular assemblies, macromolecules and components, their localization and function in vivo and at a single molecule level.
- C. Development of instrumentation, devices, and methods for detecting in real time, analyzing, and separating biologically important compounds, macromolecules, and their interactions.
- D. Development of new methods and materials directed toward the solution of biological macromolecule structures by, but not limited to, x-ray diffraction, electron diffraction, and NMR spectroscopy.
  1. New methods for the determination of the structures of membrane associated proteins.
  2. New methods for the determination of macromolecular structures in a high throughput mode, including improved detectors, data collection, automated data analysis, and faster software for structure calculations and comparisons.
3. New methods designed to improve the efficiency of beam line use at synchrotrons.
- E. Development of instrumentation for the imaging of biologically important molecules and cellular components, including but not limited to:
  1. Instrumentation and software for light microscopy.
  2. Instrumentation and software for conventional and cryo-electron microscopy, including automated apparatus for controlled and reproducible specimen preparation.
  3. Instrumentation, methods and technologies for analysis and manipulation of cells, subcellular components, and single molecules, including atomic force microscopy, atomic forceps and tweezers, and solid state (lensless) microscopy.
  4. Instrumentation, methods, technologies, and probes for spectroscopy, including magnetic resonance, fluorescence spectroscopy, and EPR.
- F. Bioinformatics, including but not limited to:
  1. Development of databases relative to structural and cellular biology.
  2. Development of methods for linking the information that might be contained in such databases.
  3. Development of new tools that might be used for "mining" the information contained in such databases.
- G. Theoretical methods for, but not limited to:
  1. Analysis of macromolecular structures.
  2. Prediction of the three dimensional structures of biological macromolecules.
  3. Improved methods for structure-based drug design.
  4. Improved methods for understanding complex systems at the cellular and organism level.
- H. Development of computerized tools that might be used in the presentation of the concepts of

cell and structural biology to audiences at a variety of levels.

### **Division of Genetics and Developmental Biology**

Research on developing a better understanding of fundamental processes and mechanisms of development and inheritance in health and disease. Support of basic topics in genetics and developmental biology, including nucleic acid chemistry, the structure of genetic material, the mechanisms of transmission and expression of genetic information, cellular regulation of growth and differentiation, molecular immunology, and population genetics. Areas that may be of interest to small businesses include, but are not limited to:

- A. Development of computer software for the analysis of the primary and secondary structures of nucleic acids as these relate to genetic problems.
- B. Improvement of methodology for oligonucleotide synthesis.
- C. Improvement in procedures for the separation and analysis of nucleic acids and proteins as these relate to genetic problems.
- D. Improvement of methodology (technology) for genetic analysis (e.g., gene libraries, cloning techniques, probes).
- E. Development of probes for detection of human genetic polymorphisms, including disease genes.
- F. Development of improved procedures for cytogenetics.
- G. Improvement in procedures (statistical, computational, laboratory) for the analysis of gene flow and gene dynamics in human populations.
- H. Development of improved vectors for gene transfer.
- I. Development of valid animal models for genetic diseases.
- J. Development of quantitative approaches to the analysis of complex biological systems.
- K. Development of new tools and models for study of the genetic architecture of complex phenotypes.
- L. Development of improved technology to scale up the growth of approved human embryonic

stem cells in culture and to regulate their differentiation state.

- M. Development of markers, reagents and tools to characterize the unique properties of approved human embryonic stem cell lines and to distinguish them from adult stem cells and more differentiated cells.
- N. Development of human embryonic stem cell lines as a primary cell type to be used as a model system for drug discovery.

### **Division of Pharmacology, Physiology, and Biological Chemistry**

Research related to the actions of therapeutics, including anesthetics, and the development of biotechnological methods for their production and investigation. Research on pain management as it relates to anesthesia and the perioperative period. Research on responses to traumatic injury, including burn injury, and methods to mitigate these responses. Research leading to new knowledge of physiological functions at the molecular, cellular, and organ systems levels. Research on the structure, function, and biosynthesis of cellular components and cellular metabolism, bioenergetics, and mechanisms of enzyme action, regulation, and inhibition. Research leading to the synthesis of new materials or development of new chemical methods to probe biological phenomena or to alter the behavior of biological systems. Examples include, but are not limited to:

- A. Methods for isolation, characterization, and production of natural and bio-engineered products.
  - 1. Metabolic engineering for the production of biochemicals through genetic and bioengineering manipulation of biosynthetic pathways.
  - 2. Biosensors for use both in vivo and in vitro in process engineering.
- B. Development of innovative synthetic chemistry.
  - 1. Catalytic asymmetric methods and methods for large-scale synthesis.
  - 2. New methods applicable to combinatorial library construction, design, analysis, and/or handling.
  - 3. Improved methods for preparation of isotopically labeled amino acids, peptides, proteins, and prosthetic groups, and therapeutic agents.

- C. Development of enzymes, catalytic antibodies, ribozymes, artificial enzymes, and host molecules as drugs or synthetic tools.
  - 1. Synthesis of suicide substrates, affinity labeling agents, and transition state analogs as potential therapeutic agents.
  - 2. New enzyme assays to reduce the reliance on radio-isotopes.
  - 3. General approaches for high throughput screening.
- D. Isolation, characterization, and development of factors involved in tissue repair and wound healing, i.e., growth factors. Tissue engineering. Development of artificial skin and skin replacements.
- E. Improved systems for collection, processing, and analysis of real time physiological data from injured or critically ill patients. Application of artificial intelligence or fuzzy logic and other methods to model non-linear behavior in critically ill patients.
- F. Systems to utilize virtual reality for surgical education and remote surgical applications.
- G. Research to improve drug design.
  - 1. Methods for understanding of structure-activity relationships.
  - 2. Mechanisms of drug-receptor interactions.
  - 3. Development of pro-drug and drug delivery strategies.
  - 4. Development of molecular diversity libraries.
- H. Research to improve drug bioavailability by improved understanding of factors that influence absorption, metabolism, transport, or clearance of therapeutics and underlying mechanisms.
  - 1. Determination of structure-activity relationships for drug metabolizing enzymes.
  - 2. Determination of structure-transport relationships for active and passive transport of drugs and metabolites.
  - 3. Research on drug transporter structure, function, and regulation.
  - 4. Development and validation of models for prediction of drug bioavailability and metabolism in humans.
- 5. Research on inter- and intra-individual differences in bioavailability.
- 6. Methods to improve sensitivity, accuracy, speed, and simplicity for measurements of drugs and their metabolites in complex biological matrices.
- I. Application of pharmacokinetic and pharmaceutical principles to the study of large biomolecules, such as proteins, polypeptides, and oligonucleotides.
- J. Development of novel targeted delivery systems for both conventional drugs and large molecules.
- K. Research to discover, detect, and understand the genetic basis of interindividual differences in drug responses.
  - 1. Identification of human polymorphisms in drug receptor and drug metabolizing enzymes.
  - 2. Methods for pharmacogenetic and pharmacogenomic analyses and their application to phenotypic and genotypic characterization of populations.
  - 3. Development of proteomic and metabolomic methodologies to support research in this area.
  - 4. Development of appropriate databases, specimen, and cell culture collections to support research in this area.
- L. Development of novel in vivo and in vitro methods to predict toxicities of pharmacologic agents.
- M. Development of differentiated hepatic cell lines from human stem cells that are equivalent to adult hepatocytes to characterize metabolic profiles of pharmacological candidates by phase 1 and 2 enzymes.
- N. Development of bioinformatic resources and/or pharmacokinetic modeling programs which utilize ADME parameters of drugs and pharmacogenomic information of individual patients or patient populations to reduce adverse drug reactions in individual patients.
- O. Development of methods for quantitating protein and lipid glycoconjugates and for determining their structures. Development of generally applicable methods for the synthesis of branched chain oligosaccharides.



- P. Development and application of methods and materials for the elucidation of membrane protein structures at or near atomic resolution.
1. Novel vector and host cell systems for over-expression of membrane proteins, in both unlabeled and isotopically labeled forms.
  2. Novel and high purity detergents and non-detergent solubilization agents for the purification and crystallization of membrane proteins.
  3. Apparatus to facilitate crystallization and manipulation of fragile crystals for data collection.
  4. Reagents for heavy atom derivatization of membrane protein crystals.
- Q. Development of high-throughput methods for sequencing and resequencing of mitochondrial genes and relevant nuclear genes and for proteomic profiling of mitochondria in diagnosis of mitochondrial diseases.
- R. Development of new metal ion chelators and other tools to probe and/or alter the localization and concentration of metal ions in cells and in whole organisms. Research to exploit metal metabolism and metal-regulated cellular control and cell-cell signaling processes to probe and/or alter cell function. Research to develop investigational and therapeutic applications of metal-complexes and to understand the factors governing their pharmacology and toxicology.
- S. Development of high-throughput methods and strategies to characterize the function of proteins and enzymes and/or define the functional interrelationships of proteins and enzymes.
- T. Development of research tools to promote scientific collaboration in any of the above areas of research. For example, applications software for secure peer-to-peer networking to facilitate the exchange of scientific data and research materials or to construct a searchable distributed database.

#### **Center for Bioinformatics and Computational Biology**

- A. Development of databases for activities that fall within the mission of NIGMS.
- B. Development of general methods for data mining.

- C. Development of tools to model complex biological systems that fall within the mission of NIGMS.
- D. Development of software for all of the above.

#### **Other Research Topic(s) Within the Mission of the Institute**

For additional information on research topics, contact:

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##### *Genetics and Developmental Biology*

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##### *Pharmacology, Physiology, and Biological Chemistry*

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#### **NATIONAL HEART, LUNG, AND BLOOD INSTITUTE (NHLBI)**

The NHLBI plans, conducts and supports research, clinical trials and demonstrations relating to the causes, prevention, diagnosis and treatment of heart, blood vessel, lung, and blood diseases and sleep disorders. The NHLBI SBIR/STTR program fosters basic, applied, and clinical research on all product and service development related to the

mission of the NHLBI. Research may be targeted to gender, race, or age subgroups.

For more specific information about areas of interest to the NHLBI, please visit our home page at <http://www.nhlbi.nih.gov>.

Research topics of interest include, but are not limited to, research and development of the following:

### Heart and Vascular Diseases

The Division of Heart and Vascular Diseases plans and directs the NHLBI's research grant, contract, and training programs in heart and vascular diseases. These programs encompass institute- and investigator-initiated basic research, targeted research, specialized centers and clinical trials. The DHVD maintains surveillance over developments in its program areas and assesses the national need for research on the causes, prevention, diagnosis, and treatment of cardiovascular disease. The DHVD ensures that effective new techniques, treatments and strategies resulting from medical research are transferred to the community through professional, patient, and public education programs in a timely manner.

The Division has three major programs: the Heart Research Program, the Vascular Biology Research Program, and the Clinical & Molecular Medicine Program, in addition to a Research Training and Special Programs Group.

*Heart Research Program.* Supports basic, applied, and clinical research in cardiac diseases, from embryonic life to adulthood.

*Vascular Biology Research Program.* Supports research in atherosclerosis, hypertension, basic vascular biology and gene therapy for the prevention and/or treatment of vascular diseases.

*Clinical & Molecular Medicine Program.* Supports clinical, basic and engineering research on cardiovascular disease and health. Its scope includes genetic, genomic and proteomic research; engineering theory and practice applied to biology and medicine including therapeutic cardiovascular devices and diagnostic instrumentation; informatics and simulation; and cohort, case-control, and randomized clinical trials.

- A. Ambulatory monitoring (long term) of blood pressure.
- B. Angioscopes with increased flexibility and enhanced resolution.
- C. Animal models for assessing genetic determinants.
- D. Anti-hypertensive drugs from natural and synthetic sources.
- E. Biological, chemical, and mechanical sensors.
- F. Biologics.
- G. Biomaterials.
- H. Biomimetics.
- I. Biotechnologies.
- J. Lipid measurements and standardization in fresh human serum, without matrix effects.
- K. Circulatory Support Systems.
  1. Artificial heart.
  2. Ventricular assistance.
  3. Automatic control.
  4. New animal models for in vivo testing.
  5. Percutaneous and transcutaneous transmission of electrical energy.
  6. Implantable rechargeable batteries and alternate power sources.
- L. Computational Biology.
- M. Computerized modeling of hemodynamics in complex congenital heart disease.
- N. Development of new and improved antisense agents for the cardiovascular system focusing on the mode of introduction; the optimal length and specificity of the oligomer; non-specific interactions with other cellular components; and the potential toxic effects and the exact mechanism of the antisense oligomer.
- O. Development of phenotypic screening methods in the mouse for heart, lung, and blood diseases and sleep disorders.
- P. Diagnostic instrumentation for the mouse and rat.
- Q. Education and video systems.
- R. Tissue Engineering. New approaches and technologies that can be used to engineer functional tissue for repair or replacement of damaged or diseased tissue.  
<http://grants.nih.gov/grants/guide/pa-files/PAR-01-006.html>.

- S. Gene and gene product relationship, structure, and function.
- T. Gene Discovery Technologies.
- U. Genetics of Complex Diseases. gene/gene and gene/environment interactions.
- V. Gene assessment and diagnostic technologies.
- W. Genomic applications and tools.
- X. Geographic sensing systems for high risk patients.
- Y. Heart failure, early detection and treatment strategies.
- Z. Informatics (bio and medical), modeling and simulation.
- AA. Imaging characterizing vessel walls and lesions.
- BB. Intermediate phenotypes in hypertension.
- CC. Luminescent dyes to measure toxic metabolic intermediates in living cells in real time.
- DD. Mathematical and computer modeling of structure, function, and electrical activity of the normal and diseased heart.
- EE. Medical imaging systems.
- FF. Medical implants (heart valves, vascular grafts, stents, pacemakers, defibrillators, etc.).
  - 1. Novel designs and materials.
  - 2. Failure prediction/analysis.
  - 3. Manufacturing.
  - 4. Monitoring.
  - 5. Preservation methods.
  - 6. Quality assurance and quality control.
  - 7. Reference biomaterials for evaluation of biocompatibility.
  - 8. Reliability.
  - 9. Biological response.
- GG. Molecular and gene imaging.
- HH. Neuro-imaging in hypertension.
- II. Non-invasive methods of detecting cardiac rejection, particularly in infants and young children.
- JJ. Non-toxic and selective molecular cages for delivering short-lived vasoactive agents to the vasculature.
- KK. Nutrition and dietary interventions, products, software and databases.
- LL. Precursors of preeclampsia, pregnancy-induced hypertension.
- MM. Preservations methods for cardiovascular tissues or organs for use in transplantation and in research studies.
- NN. Pro- and anti-angiogenic and vasculogenic genes, proteins and drugs.
- OO. Proteomics.
- PP. Radiologic phantoms mimicking the human torso.
- QQ. Magnetic resonance, x-ray, nuclear medicine.
- RR. Resuscitation-enabling technologies.
- SS. Training.
- TT. Vaccines for the prevention or treatment of atherosclerosis.
- UU. Vascular and renal tubular fluid dynamics, non-invasive assessment.
- VV. Viral and non-viral vectors for gene therapy.

### Lung Diseases

The NHLBI Division of Lung Diseases (DLD) maintains surveillance over developments in pulmonary research and assesses the Nation's need for research on the causes, prevention, diagnosis, and treatment of pulmonary diseases. Also within the purview of the Division are: technology development, application of research findings, and research training and career development in pulmonary diseases. The DLD plans and directs the research and training programs which encompass basic research, applied research and development, clinical investigations, clinical trials, and demonstration and education research. Two programs comprise the Division of Lung Diseases: the Airway Biology and Disease Program, and the Lung Biology and Disease Program.

*Airway Biology and Disease Program.* Focuses on basic and clinical research, education and training related to chronic obstructive pulmonary diseases, asthma, cystic fibrosis, control of breathing, bronchiolitis, respiratory neurobiology, sleep, and other adult airway diseases.

*Lung Biology and Disease Program.* Supports research, education, and training programs in lung cell and vascular biology; lung growth and

development and pediatric lung disease; acute lung injury and critical care medicine; interstitial lung diseases, including pulmonary fibrosis; and AIDS and tuberculosis.

#### A. Diagnostic Tools.

1. Computer algorithms for reading and comparing chest radiographs and scans (computed tomography, radioisotopes, etc.) using digitized images.
2. Diagnose and treat respiratory abnormalities during sleep in infants, children, and adults.
3. Imaging techniques to monitor lung cell functions in vivo.
4. Non-invasive measurement of blood gases, hemodynamics and respiratory function in infants, in children, and in adults.
5. Non-invasive methodologies for measuring airways inflammation in asthma.
6. Non-invasive markers of lung disease activity.
7. Non-invasive methods to detect pulmonary thromboembolism, hypertension, and edema.
8. Probes to monitor peripheral tissue oxygenation in vivo.
9. Use of ambulatory monitoring techniques to diagnose and manage respiratory disorders of sleep.
10. Computerized tomography to quantify and monitor pulmonary disease processes.

#### B. Information and Health Education Tools.

1. Computer technologies to promote adoption and implementation of asthma clinical practice guidelines in medical practice.
2. Health education methodologies for patients, families, or communities to prevent or cope with lung diseases or to reduce their impact, especially among people with asthma who are minorities or living in poverty.
3. Improve smoking cessation programs.
4. Information systems to coordinate patient management and monitoring among patients and health care professionals.

5. Interventions to reduce passive smoking in infants and children.
6. Use of interactive and computer technology to teach self management to asthma and chronic obstructive lung disease patients.
7. Health education interventions on the recognition, management, or prevention of problem sleepiness and sleep disorders for the public, physicians, and other health care professionals.

#### C. Materials and Devices.

1. Blood substitutes to improve gas exchange.
2. Emergency, portable, and servo-controlled ventilatory support devices.
3. Improved aerosol delivery systems.
4. Improved devices for continuous oxygen administration, including airline travel.
5. Improved extracorporeal or implantable devices for blood gas exchange (artificial lung).
6. New approaches and technologies that can be used to engineer functional tissue, in vitro, for replacement or repair of damaged or diseased lung tissue, in vivo.
7. Personal exposure monitors for aeroallergens and other environmental pollutants.
8. Thrombo-resistant materials for extracorporeal or implantable devices for blood gas exchange and for indwelling catheters.

#### D. Methods.

1. "Clean" animal models for *Pneumocystis carinii* infections.
2. Culture *Pneumocystis carinii* in vitro.
3. Determine viability and enumeration of infectious *Pneumocystis carinii* organisms.
4. Development and standardization of in vitro systems for the study of pulmonary epithelial (airway) cells and pulmonary endothelial (vascular) cells.
5. Identification of genes causing and modifying lung diseases.
6. Identify and detect lung cell specific differentiation markers.
7. Identify lung stem cell types.

8. Identify species and strain differences of *Pneumocystis carinii*.
9. Isolate, identify, and characterize cells found in pulmonary granulomas.
10. Methods to monitor levels of alertness or sleepiness continuously over extended periods of time.
11. Three-dimensional static, mathematical, cell culture models of airways and alveoli to define parameters determining aeropollutant absorption, deposition, and effects.
12. Develop technologies and tools for use in genomic or proteomic investigations of pulmonary diseases.

#### E. Treatments.

1. Delivery of specific drugs (e.g., antioxidants, artificial proteinase inhibitors, surfactant) to the lungs for treatment of pulmonary and non-pulmonary diseases.
2. Gene therapy for cystic fibrosis, alpha1antitrypsin deficiency, primary pulmonary hypertension, and other inborn errors of metabolism affecting the lungs.
3. Improved aerosol delivery systems.
4. Novel pharmacologic and gene therapy approaches for asthma, acute lung injury, idiopathic pulmonary fibrosis, and bronchopulmonary dysplasia.
5. Novel pharmacologic approaches for treatment of sleep apnea.
6. Pharmacological means of stimulating growth and repair of alveoli and reparative or restorative elastogenesis in lungs suffering emphysematous changes.

### Blood Diseases and Resources

The NHLBI Division of Blood Diseases and Resources (DBDR) plans and directs an integrated research and training program, with an emphasis on non-malignant blood diseases such as Cooley's anemia, sickle cell disease, hemophilia, hemochromatosis, and disorders of hemostasis and thrombosis. A program in hematopoietic stem cell biology and transplantation focuses on use of transplantation to treat blood diseases, coordination of clinical transplant research, and identification of new research opportunities. The Division also has a major responsibility to improve the adequacy and

safety of the nation's blood supply through research in transfusion medicine.

Two programs comprise the DBDR, the Blood Diseases Program, and the Blood Resources Program.

***Blood Diseases Program.*** Supports research and training in nonmalignant disorders of blood cells and the hematopoietic system.

***Blood Resources Program.*** Supports research and training in blood and marrow transplantation, thrombosis and hemostasis, and, transfusion medicine.

#### A. Animal models for blood diseases such as:

1. Fanconi anemia.
2. Hemophilia.
3. Hereditary hemorrhagic telangiectasia.
4. Paroxysmal Nocturnal Hemoglobinuria.
5. Platelet diseases.
6. Sickle cell disease.
7. Thalassemia.
8. Thrombocytopenia.
9. Thrombosis and thrombolysis.
10. von Willebrand disease.

#### B. Assays, especially hi-throughput technologies for:

1. Anti-thrombotic drug monitoring.
2. Assays to detect Creutzfeldt-Jacob Disease (CJD).
3. Automated screening of therapeutic agents for sickle cell disease.
4. Blood coagulation factor abnormalities.
5. Blood-borne infectious agents transmitted by blood transfusion.
6. Hematologic components of hematopoietic growth factors and cytokines.
7. Human hematopoietic stem cells and mesenchymal (stromal) stem cells plus stem cells with the potential to differentiate into blood cells.
8. Human leukocyte antigen (HLA) typing for stem cell transplantation.
9. New platelet functional tests.

10. Predictors of autoimmune and alloimmune response.
11. Thrombosis screening.
12. von Willebrand disease.
13. Iron overload or status.
- C. Drugs to Treat Hematologic Diseases and Cytopenic States
  1. Anti-coagulants.
  2. Anti-thrombotic agents.
  3. Anti-inflammatory agents.
  4. Anti-sickling agents or other pharmacologic approaches to sickle cell disease.
  5. Fetal hemoglobin enhancing agents.
  6. Fibrinolytic and anti-fibrinolytic agents.
  7. Iron chelators.
  8. Replacement agents for hematologic factor deficiencies.
  9. Therapeutic uses for plasma derivatives.
  10. Anti-cytokines.
  11. Anti-metalloproteinases.
- D. Equipment and procedures for the collection, separation, processing, preservation, storage, and distribution of blood and blood components.
- E. Tissue Engineering: New approaches and technologies that can be used to engineer functional tissue for repair or replacement of damaged or diseased tissue.  
<http://grants.nih.gov/grants/guide/pa-files/PAR-01-006.html>.
- F. Gene therapy vectors and delivery systems for the treatment of hematologic genetic diseases.
- G. Health education programs to prevent or reduce the impact of blood diseases.
- H. Management and education systems for more effective and appropriate use of blood products.
- I. Methods/technologies for:
  1. In vitro inactivation or removal of microorganisms from blood, blood components, and plasma derivatives.
  2. Isolation, purification, expansion, and storage of hematopoietic stem cells and mesenchymal (stromal) stem cells plus stem cells with the potential to differentiate into blood cells.
3. Methods/instrumentation for continuous, real-time measurement of blood flow or stasis.
4. Measuring iron non-invasively.
5. Non-invasive measurement of blood cell counts or other blood components.
6. Platelet storage methods that preserve biological efficacy.
7. Prolonging the in vivo lifetime of transfused red cells for therapeutic uses.
8. Reducing the loss of blood in neonates to phlebotomy.
9. Screening and prenatal diagnosis of inherited blood disorders.
10. "Silencing" the abnormal b-globin gene(s) in the hematopoietic stem cells of individuals with sickle cell disease.
11. Synthesizing, screening, and evaluating the safety and efficacy of therapeutic oxygen carriers.
12. Synthesizing or purifying plasma proteins for therapeutic use.
13. Techniques for improving exchange transfusions for sickle cell disease patients.
14. Testing potential anti-sickling agents.
15. Carbohydrate composition and analysis of glycoconjugates.
16. Multiplexed microassay system for hemostatic factors, cytokines, and inflammatory markers.
17. Intravascular imaging techniques for thrombosis.
18. Non-invasive imaging for intravascular atherothrombosis.
19. Portable analyzer for clinical application.
20. Real time in vivo imaging for thrombosis and thrombolysis.
- J. National reference laboratory to identify unusual hemoglobinopathies or coagulation disorders.
- K. Public Health Education.



1. Computer-assisted personal interview (CAPI) for the blood donor screening process.
  2. Computerized health education programs in: blood, platelet and bone marrow donations.
  3. Tutorials for community-based providers: emerging technologies.
- L. Tools, reagents, and assays for hematologic research in mouse and other animals.
1. Imaging devices.
  2. Micro-surgical instruments.
  3. Polyclonal and monoclonal antibodies.
  4. Recombinant and purified proteins.
  5. Micro-acquisition and micro-analytical tools for samples.
- M. Prothrombotic and hemorrhagic biomarkers.
- N. Computational approaches to gene environment interaction in hemostasis.
- O. Computer-based algorithm to diagnose thrombotic or hemorrhagic risks.
- P. Bioinformatics to store and analyze genes, proteins, and biomarkers for hemostasis.

### **Epidemiology and Clinical Applications**

The NHLBI Division of Epidemiology and Clinical Applications (DECA) plans and directs programs in epidemiologic studies, basic and applied behavioral research, demonstration and education research, and projects for disease prevention and health promotion, including large scale clinical trials. The research supported by the Division provides multidisciplinary approaches to heart and blood vessel, lung, and blood diseases, with a primary focus on cardiovascular disease.

DECA is comprised of two programs, the Clinical Applications and Prevention Program and the Epidemiology and Biometry Program, and the Office of Biostatistics Research.

*Clinical Applications and Prevention Program.* Supports research into prevention of heart and vascular, pulmonary, and blood diseases through activities such as clinical trials, health promotion/disease prevention trials, community intervention studies, health education research, nutrition research, and behavioral medicine research.

*Epidemiology and Biometry Program.* Supports and conducts epidemiological studies of heart and vascular, lung, and blood diseases in defined populations in the United States and other countries.

- A. Clinical research/intervention studies designed to improve cardiovascular disease outcomes.
- B. Clinical trial methodologies.
- C. Communication techniques for minority and low-income populations.
- D. Community and demonstration programs.
- E. Cardiovascular disease information, education, prevention, and treatment systems for primary caregivers.
- F. Interactive databases.
- G. Measures of patient adherence/compliance.
- H. Methods for:
  1. Lifestyle intervention.
  2. Matching patients to lifestyle, intervention, or treatment.
  3. Quantitative measurement systems for behavioral and lifestyle variables, e.g., diet and physical activity.
- I. Models of behavior modification
- J. New agents or treatment strategies.
- K. New assay systems/techniques to measure patient responses.
- L. New materials and equipment for enhanced medical Imaging systems.
- M. New methods for communication of research results.
- N. Novel/unique methods for collection, transmission, management and analysis of clinical data.
- O. Nutrition, physical activity, smoking, stress and tobacco cessation interventions.
- P. Nutrition and physical activity measurement methods.
- Q. Pharmaceutical development and toxicologic evaluation.
- R. Population tracking mechanisms.
- S. Psychosocial measurement instruments, especially in minority populations.
- T. Prognostic assays.

- U. Quality of life measurement and analytic methods.
- V. Software for:
  1. Clinical trials.
  2. Epidemiology studies.
  3. Literature abstracting.
  4. Meta-analysis
  5. Statistical analysis.
  6. Shared decision making.
- W. Screening, assessment, and tracking tools for hypertension, coronary heart disease, heart failure and other cardiovascular risk factors and diseases.
- X. Survey questionnaires.
- Y. Training techniques and modules.
- Z. Interactive web-based programs for health promotion.
- AA. Computerized systems to support evidence-based clinical practice in prevention and treatment of hypertension, coronary heart disease, heart failure and other cardiovascular risk factors and diseases.

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**NATIONAL HUMAN GENOME RESEARCH INSTITUTE (NHGRI)**

The Human Genome Project (HGP) is an international initiative involving the NIH and several other federal, private, and international organizations. At the NIH, the NHGRI is the lead institute for the HGP. Many of the initial goals of this project—genetic and physical maps of the mouse and human, and the DNA sequences of *E. coli*, *S. cerevisiae*, *C. elegans* and *D. melanogaster*—have been realized. A working draft version of the human sequence was published in the winter of 2001, and the finished, high quality human sequence will follow within the next couple of years. Ninety-five percent (95%) coverage of the mouse genome was obtained by May 2001 and the complete genome will be sequenced by 2005.

Once the DNA sequence of an organism becomes available, many new avenues to studying its biology, and the biology of other organisms through comparative genomics, are opened. However, new and improved research tools, approaches, and capabilities are needed to discover and use the vast

amount of biological information in complete genomic DNA sequences. In 1998, a set of new goals was adopted for the U.S. Human Genome Program (see Goals at <http://www.nhgri.nih.gov/98plan/>). In addition to completing the human and mouse maps and sequences, the aim of the NHGRI research program was extended to developing new technological approaches that will be necessary to understand and use genomic DNA sequence. Therefore, important areas of attention for the NHGRI will be the continued development of new technology for mapping and sequencing; for the interpretation of genomic sequence, including functional analysis of non-coding sequences; for the study of sequence variation; and for the analysis of gene expression. Support for scholarly research as the foundation for understanding the ethical, legal and social implications (ELSI) of genomics and genetics research will also continue to be a major area of emphasis.

The success of the Human Genome Project has been due in large part to the development of improved technologies, strategies and methods that can be applied on a genome-wide scale in a cost-effective manner. As part of its interest in continuing to provide support for technology development research, therefore, the NHGRI solicits SBIR/STTR grant applications in the areas listed below. Innovative approaches in other areas not listed in the major topics below will also be seriously considered.

### **DNA Sequencing**

Development of (1) innovative technologies and strategies that promise to reduce the cost, increase the throughput, or improve the accuracy of large-scale DNA sequencing of complex genomes; (2) strategies and technologies for obtaining DNA sequence in the gaps that are left by current sequencing methods or that will improve the efficiency of sequencing in genomic regions that have proved difficult to sequence due to limitations in available cloning and sequencing technology; (3) innovative technologies, cost-effective technologies for determining sequence in regions of difference between closely-related organisms; and (4) instrumentation and methods development, from technical feasibility through prototype development and introduction into production. Any applicable technology is welcomed; micro- and nanotechnology approaches are particularly encouraged.

### **Human Genome Sequence Variation**

Development of new or improved methods and analytic tools for: (1) the large-scale identification, scoring, and interpretation of DNA sequence variants; (2) the identification of haplotypes and generation of haplotype maps; and (3) facilitation of studies relating the distribution of variation to association with disease, to gene mapping, and to an understanding of chromosomal and population processes.

### **Comparative Genomics**

Improvement in the technology for generating clone libraries useful for genomic analysis with DNA inserts that are stable, free of artifacts, and faithfully representative of genomic DNA from complex organisms. Also of high priority is the development of technology to generate physical maps efficiently and rapidly.

### **Functional Genomics**

Development of new or improved technologies for large-scale or genome-wide approaches relating to: (1) gene discovery, full-length cDNA synthesis, or gene expression analysis; (2) analysis of the products of gene expression (e.g., proteins, metabolites), their identification in biological samples, their modifications, their interactions; (3) functional analyses of non-coding sequences; and (4) generation and detection of mutations. Any applicable technology is welcome; micro- and nanotechnology approaches are particularly encouraged.

### **Bioinformatics and Computational Biology**

Development of new or improved tools for: (1) obtaining, representing, analyzing and archiving data and (2) improving databases, in the areas of DNA sequence, gene mapping, complex trait analysis, genetic variation and homology, and functional genomics.

### **Ethical, Legal and Social Implications (ELSI) of Genomics and Genetics Research**

Examination of: (1) the issues surrounding the completion of the human DNA sequence and the study of human sequence variation raised by the integration of genetic technologies and information into health care and public health activities; (2) the integration of knowledge about genomics and gene-environment interactions into non-clinical settings;

and (3) issues surrounding the commercialization of genetic technologies, including issues relating to patenting, licensing, and other intellectual property concerns.

### **Other Research Topic(s) Within the Mission of the Institute**

Individuals interested in any of the above listed areas are encouraged to contact the NHGRI staff listed below. For more specific information about areas of interest to the NHGRI, please visit our home page at <http://www.genome.gov/Grants/>.

For additional information on research topics, contact:

#### *All Research Topics Except ELSI*

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### **NATIONAL INSTITUTE OF MENTAL HEALTH (NIMH)**

The mission of the National Institute of Mental Health (NIMH) is to diminish the burden of mental illness through research. To achieve this goal, the NIMH funds basic research, clinical studies, and services delivery research concerning any aspect of behavioral and mental disorders (including HIV prevention and neuro-AIDS research). Ultimately, this research will lead to greater understanding, better treatment and rehabilitation or prevention of mental disorders. The NIMH is also concerned with the speedy dissemination and use of this knowledge through scientific communications and public education, and in its more effective implementation in practice and service delivery systems. There is a general need to develop reliable and inexpensive

equipment, and other products, that can serve these needs.

For additional information about areas of interest to the NIMH, please visit our home page at <http://www.nimh.nih.gov>.

### **Division of Neuroscience and Basic Behavioral Science**

Through research in neuroscience and basic behavioral science we can gain an understanding of the fundamental mechanisms underlying thought, emotion, and behavior and an understanding of what goes wrong in the brain in mental illness. Research sponsored by the Division of Neuroscience and Basic Behavioral Science covers a broad range of neuroscience topics: from both experimental and theoretical approaches, from molecules to whole brains to populations of individuals, from single cell organisms to humans, from across the entire lifespan, and from states of health and disease. This division also supports research on the basic behavioral, psychological, and social processes that underlie normal behavioral functioning. The topics listed below reflect the NIMH interest in technologies related to this broad range, but should not be considered to be a complete list. Prospective applicants are strongly encouraged to contact Dr. Michael Huerta (listed below) with questions about the relevance of their interests to the mission of this division.

A. **Cutting-Edge Technologies for Neuroscience Research.** Most of the research topics listed after this one are posed from the Division's neuroscience and basic behavioral science mission-oriented perspective, however, the technologies that might be developed to address those mission goals might be quite fundamental. Prospective applicants familiar with such technologies, but not familiar with the mission-related use of these technologies, are strongly encouraged to contact Dr. Michael Huerta (listed below) for assistance in bridging this gap between their technical knowledge and knowledge of the neuroscience-related mission of NIMH. Technologies and approaches that might be used in products relevant to this mission include, but are not limited to:

1. **Caged Molecules.** These could be activated, or release an active agent, when specified bonds are broken by chemical, biochemical, photic, or other means. Among other uses, such molecules could

be used to indicate biochemical or physiological processes or to deliver pharmacologic substances to highly localized brain regions.

2. **Genetically Engineered Proteins.** Such proteins could be put to any number of uses, including to express a fluorophore or chromophore at the occurrence of specific biochemical processes to report the time and location of such processes in brain tissue.
  3. **Inducible Gene Expression.** Methods to turn on or off expression of particular genes in transgenic animals on the basis of time in the lifespan, location in the brain, or other factors. Such a capability would significantly advance basic brain research, and would have important implications for treatment and therapy of mental illness.
  4. **Combinatorial Approaches.** These are high-through-put approaches that can be used to screen and synthesize molecules that affect brain cells.
  5. **Biocompatible Biomaterials.** Such research and development relates to the chronic use of electrodes and other probes used in brain research, as well as implanted drug delivery devices.
  6. **Nanotechnologies.** This emerging area of technology presents a wide range of opportunities for brain research, from the fabrication of probes to monitor brain physiology to novel means of delivering drugs and other substances.
  7. **Informatics Tools.** Such technologies allow brain scientists, clinicians and theorists to make better sense and use of their data. These tools and approaches include those to acquire, store, visualize, analyze, integrate, synthesize and share data, including those for electronic collaboration.
  8. **Simulation Technologies.** Computer-based simulations of parts of neurons, neurons, circuits or even organisms to observe the manner in which these components interact. For example, simulations of individual organisms with constellations of particular traits that vary across individuals would allow analysis of their interactions and their impact on the population as a whole.
  9. **Mathematical and Computer Algorithms.** Such algorithms could be used to analyze large and/or complex data sets. Among other applications, these could be used to segment images (obtained from electron or light microscopes, or from volumetric imaging instruments such as confocal microscopes and magnetic resonance imagers), filter noise, visualize data or search vast data sets for specified patterns or data (e.g., use of pattern recognition algorithms to search time series data sets obtained from electrophysiological recording of neural activity, or video data obtained from behavioral analysis of genetically altered animals).
  10. **Telemetry.** Transferring data from one point to another is important for neuroscientists monitoring the physiological signals from the brain. Telemetry, even over relatively short distances (from a few millimeters to a few meters), could, for example, provide a means to obtain data from awake, behaving animals without interfering with the behavior of interest.
  11. **Biosensors.** Neurons communicate with each other through thousands of different chemical substances; internally, molecular pathways direct the function of the neuron. Sensors of high specificity and sensitivity for such substances would provide neuroscientists with important new ways to study the brain.
- B. **Instrumentation for Basic and Clinical Neuroscience Research.** Modern equipment that uses the most recent technological advances is needed in neuroscience research so that neural substrates of mental illness can be identified and localized. The NIMH is interested in supporting research and development of new or improved approaches relevant to, but not limited to, the following:
1. **Neurophysiology.** Microelectrodes, smart nanoscaffolds, macroelectrodes, biocompatible coatings, interfaces to electronics, software for data analysis, visualization, etc.
  2. **Cell Sorting.** Based on cell size, type, function, etc.
  3. **In Vivo Electrochemical Voltammetry.** More sensitive and selective electrodes, software for data analysis, etc.

4. High Performance Liquid Chromatography. Improved reliability, specificity, sensitivity, etc.
  5. Technology to support Multiple Unit Recording Electrode Arrays. Both recording techniques and analysis techniques.
  6. Physiological and Behavioral Monitoring. Temperature, activity, sleep duration, neuronal activity, EEG activity, EKG, pulse rate, recording, capture and analysis of multiple single unit activity from microelectrodes.
  7. Associated Software.
- C. **Macroscopic Neuroimaging**. Modern technologies allow for the observation of the structure and function of the intact brain. This capability has the potential to greatly advance understanding of the brain in both health and disease, and across the lifespan. NIMH is interested in advancing this area of technology through enhancing current tools and approaches, as well as developing entirely new ways to image the brain. All modalities are of interest, including, but not limited to: magnetic resonance imaging (MRI) or spectroscopy, positron emission tomography (PET), optical imaging or spectroscopy, single photon emission computed tomography, magnetoencephalography (MEG), diffusion tensor imaging (DTI), etc. Due to its greatly increased use in recent years, technologies specifically focused on improving the utility of fMRI techniques are of particular interest.
1. Innovative agents and/or technologies to visualize brain connectivity in situ with minimal invasion.
  2. Improvement in the techniques, the design and construction of devices for non-invasive imaging for any modality, for example, improving spatial resolution, quantitative accuracy, signal-to-noise ratio, and electronics.
  3. Development and enhancement of non-invasive imaging techniques for evaluating alterations in brain physiology produced by drugs. These would include techniques for monitoring changes in regional blood flow; concentrations of tissue metabolites; and the distribution and activity of receptors.
  4. Synthesis, or isolation from natural products, of highly selective receptor ligands or indicators of neurochemical processes, which would be labeled for imaging by one or more particular modality.
  5. New approaches in radiochemistry that will permit more exact identification of the chemical changes associated with behavioral states (e.g., sleep or arousal) or mental illness as observed with any particular neuroimaging modality.
  6. Better tools and approaches for producing isotopes and other chemical agents used in neuroimaging.
  7. Synthesis of molecules containing stable, rarely occurring isotopes designed to be detected by non-invasive imaging techniques (e.g., fluorine-containing molecules, carbon-13 labeled substrates).
  8. Automated interface systems for handling PET radiopharmaceuticals; oxygen-15 and other isotope-based radiopharmaceuticals have limited use because of the difficulty in handling the isotope.
  9. Methods and associated products for quantitation of imaging data including new statistical approaches for evaluating the data.
  10. Methods to integrate routines for greater and more precise computer enhancement of the images, and for combining or overlaying images obtained from multiple modalities.
  11. Software needed for the precise quantitation of data obtained from these imaging techniques with emphasis on the reliable definition of discrete, anatomically distinct areas within the brain.
  12. Novel agents or other tools to increase the ability to correlate features of MRI images with histological features (e.g., cytoarchitecture or chemoarchitecture) both identified and those yet to be identified.
  13. Generation of physiologic measurements from images of regional radioactivity generated during PET, especially for the study of brain neurotransmitter/neuroreceptor systems.
  14. Novel approaches to visualizing data obtained in neuroimaging, such as the computational "unfolding" of three-dimensional images of cerebral cortex.



15. Improved methods for pediatric brain imaging. These would include: software and database products, equipment for creating a "child-friendly" environment and for the behavioral training of children and impaired subjects for cooperation and motion reduction during neuroimaging procedures.
16. Combining of different imaging technologies (e.g., ERPs and fMRI; MEG and fMRI; MEG and EEG, etc).
17. Development of equipment, software and other tools for recording and quantifying eye movements, motion, and autonomic reactivity during scanning, applicable to all ages (including young children), particularly in the MRI environment.
18. Methods for relating changes in brain morphology and and metabolism associated with age, particularly infancy through adolescence, to changes in hemodynamic responses to neural activity and fMRI signals.

D. **Microscopic Neuroimaging.** The morphology of individual neurons and the distribution of subcellular components within them, are key to understanding the manner in which these cells function. Advances in the development of agents indicating neuronal structure and function that can be visualized microscopically are important to the NIMH's interest in brain research. This includes enhancements of current agents and ligands to be imaged (agents indicating specific biochemical processes or structures, etc.); development of novel agents and ligands; software to assist interaction with the data; and other related technologies and methods. Examples would include, but not be limited to:

1. Software and hardware for analyzing image data obtained by microscopes, including tools to automatically or semi-automatically. Identify particular profiles (e.g., labeled cell bodies), segment images, reconstruct images into three dimensional representations, perform unbiased counting and measuring, etc.
2. Synthesis and testing of novel or improved probes for microimaging the nervous system.

E. **Molecular and Cellular Neurobiology and Neurochemistry.** Manipulating and studying

basic molecular, cellular and chemical processes has led to insight to understanding brain function, and has provided the foundation on which pharmacological interventions have been developed for the treatment of mental illness. NIMH is interested in supporting a wide range of new techniques and tools related to this area. These include, but are not limited to:

1. New low-cost techniques for hybridoma production of monoclonal antibodies specific for "neural antigens" (e.g., neurotransmitters, small peptides, neurotransmitter receptors).
2. Innovative methods for establishing a "monoclonal bank" (frozen cells) for each of the cell lines as a permanent, widely available, reliable, and low cost source of monoclonal antibodies for research on the nervous system.
3. Labeled antibodies or other agents that will readily identify receptors for which there are no ligands (orphan receptors) and which have low densities in the brain.
4. Automated methods for quantitating the low levels of bound ligands for quantitating receptors that are sparsely scattered in the brain.
5. New cell lines that express each of the known neurotransmitter receptors so that each cell line will be homogeneous for one receptor.
6. New cell lines that express each of the above receptors linked to some metabolic function and/or second messenger so that the functional consequences of receptor occupancy can be detected.
7. High volume, inexpensive assay methods for measuring both receptor occupancy and cellular response for each of the receptor types.
8. Develop cell culture models for neurons, including methods of purifying homogeneous populations of non-transformed cells by, for example, developing markers to identify neuronal cell types for use in characterizing cell-type-specific signaling pathways which may be useful in tracking the effects of various drugs.
9. Develop techniques for either activating or deactivating specific ion channels,

receptors and signal transduction pathways.

10. Develop dynamic biochemical and imaging assays that allow measurement of variables now obtained only through electrophysiological techniques.
11. New approaches to study the multiple functions of particular proteins.
12. Tools to study post-translational changes in proteins in specified tissue compartments.
13. Technologies to study functional entities within cells (e.g., green fluorescent protein approaches).
14. Tools and approaches to study coordinate changes in genes and their functional relationship to phenotypes, including phenotypes associated with specific brain disorders.
15. New ways to assess quantitatively transcription of genes in real time in a manner that is minimally injurious to cells (e.g., non-permeabilizing approaches).
16. Novel tools and approaches to study protein-protein interactions, especially those with phosphoproteins. Further develop methods and reagents for studying the structures of membrane proteins at atomic resolution. Membrane protein systems that are of particular interest to NIMH include proteins involved in normal function and pathology of cells (neurons and glia) in the central and peripheral nervous system.

F. **Genetic and Transgenic Technology.**

Advances in genetic and transgenic technologies offer many opportunities to probe fundamental questions about the brain, behavior and pathology. NIMH is broadly interested in these areas; some examples of topics relevant to the mission of this Institute include, but are not limited to:

1. Methods to perform site-directed mutagenesis in cell lines for the study of membrane proteins such as ion channels and neurotransmitter receptors.
2. Development of gene “knockout” or “knockin” animals using such approaches as homologous recombination targeting genes important in neurotransmission, development, and tropic interactions as

well as in generating behavioral models of disease.

3. New methods to delete or alter targeted genes in the preparation of transgenic animals including methods that increase or decrease gene expression.
  4. Development of new techniques and apparatus for delivery of antisense oligonucleotides into cells and specific tissue such as the brain.
  5. Develop standardized behavioral tests to assess the gene knockouts and/or gene “knockins” affecting neurotransmission.
  6. New approaches for cell-specific, tissue-specific, age-specific, transient gene activation and/or inactivation.
  7. Innovative technologies to study gene function and expression.
  8. Development of embryonic stem (ES) cell lines from rodent strains (rats and mice) of relevance to behavioral research.
  9. Development of technologies and approaches to facilitate the collection and distribution of ES cell lines containing mutations of potential relevance to behavioral research.
  10. Develop methods for long-term storage of transgenic germ cell lines.
  11. Develop technologies and approaches to aid in the renewal of founder colonies of transgenic mice from repositories of transgenic germ cell lines.
  12. Develop databases on neurobiological transgenic animals produced to date, including information such as the origin of the transgenic animal, key features of the biological and behavioral mutant, availability and location of germ cell lines, and existence of breeding colonies.
  13. Develop gene transfer technologies such as viral vectors to produce long-term, stable gene expression in the brain.
- G. **Neuroimmunology.** Research on the interplay between the brain, neuroendocrine system, and, immune system has revealed important links between these major homeostatic system components. Examples of NIMH-relevant topics in this area include, but are not limited to:

1. Development of new tools to explore the special properties of the blood-brain barrier responsible for the selective delivery or retention of cytokines, immune cells, and drugs affecting immune activity in the brain.
2. Development of assays for identifying potential autoimmune components of psychiatric disorders (other than the usual screening for “markers”).
3. Identification of critical molecules, processes, and pathways mediating signals from the peripheral immune system to the brain.
4. Development of novel cytokine ligands and antagonists.
7. Strategies for evaluating pharmacological agents (e.g., animal behavioral testing, computer simulation) on cognitive function.
8. Behavioral “models” similar in animals and humans; behavioral pharmacological effects that may serve as “surrogate” markers in humans.
9. Development of novel drug delivery systems.
10. Tools for Drug Development including neuroimaging (e.g., radiolabeled compounds) and development of animal models.
11. Pharmacological profiling (in vitro and in vivo) for potential therapeutic drugs.
12. Methods for evaluation of long-term effects of psychotropic drug administration.
13. Improving existing, and developing new, vectors for delivery of genes to the brain.
14. Development of novel therapeutic approaches based on drug-induced changes in gene promoter activity.
15. Development of novel high throughput blood-brain barrier permeability assays.
16. Development of novel molecular targets for drug development to treat mental illnesses.

H. **Pharmacology.** Pharmacological intervention represents a major force in the treatment of mental illness, and NIMH is interested in supporting research and development in this area. Relevant topics include, but are not limited to:

1. New chemical entities with high, selective affinities for each of the receptors in the brain.
2. Methods to evaluate old and new chemical entities (including complex mixtures of crude extracts from natural products) for possible therapeutic usefulness using “in vitro” and “in vivo” assays and model systems.
3. Methods for extraction, fractionalization, and isolation of active compounds from natural products. Water-soluble compounds are of particular interest due to the difficulty of the procedures.
4. Computer algorithms that model receptors to evaluate theoretical permutations of known molecules to find the molecule with the maximum probability of having the highest affinity for a specific receptor as well as those that have the potential for the most desirable “on” and “off” rates.
5. Computer models of the blood brain barrier and evaluate potential and actual drug molecules for their ability to cross or penetrate this barrier.
6. Development of new animal tests/behavior with potential value for evaluating psychotherapeutic properties of drugs.

I. **Tract Tracing Methods and Tools.** Little is known about the details of the connectivity of the human nervous system, because the best tract tracing techniques are invasive and require the deposit of substances in vivo. Methods that would be applicable to post-mortem tissue would allow significant progress in connectional studies of human tissue, as well as non-human tissue, particularly with regard to the development of connections and the connections of structures not easily accessed in vivo.

J. **Basic Behavioral Science.** It is important to develop reliable methods that can correctly identify the normal and abnormal components of cognitive, emotional, and psychosocial behavior in human development. Computer-based methods of accomplishing this are also needed to increase the accessibility and reliability of information made available to the research community.

1. **Methodological Research And Development.** There is a need to devise

new ways of data collection, analysis, management and dissemination. The goal is to encourage research that will improve the quality and scientific power of data collected in the behavioral and social sciences, relevant to the mission of NIMH. Research that addresses methodology and measurement issues in diverse populations, issues in studying sensitive behaviors, issues of ethics in research, issues related to confidential data and the protection of research subjects, and issues in developing multidisciplinary, multimethod, and multilevel approaches to behavioral and social science research is particularly encouraged.

- a. Improve or create new video devices to monitor animal and human behavior and ease analysis of behavior.
  - b. Computer software to ease analysis of behavior monitored by video or telemetry systems.
  - c. Innovative computer-based observation techniques, and computer software and hardware that allow on-line methods for characterization of interpersonal interactions in groups.
  - d. Low cost microcomputer software for the recording and analysis of patterns and sequences in observed social interactions.
  - e. Causal modeling methodology as applied to correlational longitudinal data sets.
  - f. A data translation and communication package for collecting, archiving, and making available existing longitudinal behavioral sets to the scientific community for secondary or meta-analyses.
  - g. Flexible user-friendly software for control of timed, multi-modal stimulus presentation and response collection for experiments on perception and cognition.
  - h. There is a need for the development of hardware for time-stamped diary collecting instruments for use in actigraph studies of circadian rhythms in children and adolescents. Diaries are critical for the evaluation of activity data, and time-stamped diary collecting instruments can ensure investigators of receiving reliable information.
- i. Web-based software tools for designing, updating, sharing, linking, and searching databases containing detailed information about the methodology and results of behavioral science studies.
2. Diagnosis and assessment of emotional and psychological states such as automated methods to detect specific emotional states using behavioral and autonomic indicators.
  3. Instrumentation and equipment that uses the most recent technological advances is needed so that mental disease can be related to dysfunction(s) of the CNS. Once these dysfunctions are identified and localized, rational therapies can be developed and evaluated.
    - a. Physiological Monitoring. Techniques and equipment for continuous monitoring of physiological data (e.g., temperature, activity, sleep duration, EEG activity, ECG, pulse rate). Computer programs that can record, catalog, categorize and identify interrelationships between several of the above measures. Appropriate areas for behavioral clinical research would include developing:
      - i. Reliable non-invasive means of chronic monitoring of physical activity and physiological measures such as body temperature.
      - ii. New techniques for electrophysiological images from the level of the single cell and surface EEG recording on the scalp.
      - iii. Small, portable automated systems to monitor eye function (e.g., pupil size, accommodation) and eye movements.
      - iv. Software and hardware analyzing and providing experimental control over multiple single unit recordings, on-line and in real-time.
    - b. Measurements of Infant Development Using Physiological and Behavioral Measures.

- i. Psychophysiological measures to evaluate infants during the first six months of life.
- ii. Miniaturized non-invasive instruments to record psychophysiological data (e.g., heart and respiration rate, galvanic skin response, and defensive motor behavior).
- iii. Telemetry capability for non-invasive devices so that infants can be monitored for prolonged periods without interfering with their behavior.
- iv. Computer programs and inexpensive computers that will collect, analyze and identify recurring patterns in the psychophysiological measure(s) of interest.

c. *Behavior Monitoring and Analysis.*

K. **Educational Tools.** Neuroscience and basic behavioral science area compelling areas of science that not only touches upon a diverse array of disciplines, but also provides insights to the essence of what it is to be human. Products aimed at teaching the substance of these fields to students of all ages would be useful in disseminating this information and these insights. Examples include, but are not limited to: software and other interactive media used to convey fundamental concepts about the brain to children; computer simulations of neuroscience experiments; updateable media that presents state-of-the-art information on particular topics for use by experts; website or other online, interactive electronic vehicle to allow for sharing of information about the brain and its functions, including technologies for holding interactive research conferences related to basic behavioral sciences, basic neuroscience, or clinical neuroscience.

L. **Neuroinformatics.** Data generated by brain research are diverse, vast, and complex. The diversity of data is due to the fact that neuroscience data are obtained from: theoretical, experimental and clinical approaches; from levels of biological organization that span molecules to populations of individuals and from single-cell organisms to humans; and from states of health, disease, and models of disease. The quantity of data in

brain research is the result of tens of thousands of neuroscience laboratories working around the world. The complexity of data reflects the high level of interconnectedness of the data, and their high dimensionality. Neuroinformatics is a new area of science that draws upon neuroscience, information science, computer science, statistics, applied mathematics, and a variety of engineering fields to develop tools that will let neuroscientists make better sense and use of their data. These tools include software and hardware for digital data acquisition, visualization, analysis, integration, and sharing (e.g., through tools for electronic scientific collaboration). Such tools can address data of any type or from any area of neuroscience; examples include, but are not limited to:

1. Databases, querying approaches, and information retrieval tools for neuroscience and neuroscience-related data.
2. Tools for neuroscience data visualization (and other forms of presentation) and manipulation (probabilistic atlases of brain structure or function, new statistical approaches for analyzing data, etc.).
3. Software for integration and synthesis of neuroscience data (computational models of neurons to integrate data about structure and function, environments to merge data from multiple imaging modalities, etc.).
4. Tools for electronic collaboration to allow neuroscientists to interact with colleagues, data, and instruments at a distance (this could include novel types of "groupware", etc.).
5. Tools that bridge existing neuroscience and biology information tools and resources, such as databases and informatics tools associated with genome mapping efforts.

For further information on basic and clinical neuroscience or basic behavioral science research topics, contact:

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### **Division of Mental Disorders, Behavior and AIDS**

The Division of Mental Disorders, Behavior and AIDS is responsible for planning, directing and supporting programs of research, research training, research dissemination and resource development in behavioral science, developmental psychopathology, prevention and early intervention, and in research on the causes of and prevention of HIV (AIDS). The division is comprised of the Center for Mental Health Research on AIDS and three branches. These branches are: The Developmental Psychopathology and Prevention Research Branch; the Adult Psychopathology and Prevention Research Branch and the Health and Behavioral Science Research Branch. Their respective functions are as follows:

**Center for Mental Health Research on AIDS.** This Center plans, coordinates, and supports biomedical and behavioral research designed to develop a better understanding of the biological and behavioral causes of HIV (AIDS virus) infection, and more effective mechanisms for the diagnosis, treatment, and prevention of AIDS. The Center is also interested in identifying and addressing behavioral issues in vaccine trials and in identifying the effects of HIV infection on the central nervous system.

**Developmental Psychopathology and Prevention Research Branch.** The focus of this branch is on: risk/protective factor identification; early social, emotional and cognitive developmental processes leading to psychopathology or resilience and the translation of risk and developmental research into new prevention, early intervention and treatment strategies. Studies may address modifiable and potent individual, social, cultural and environmental factors and processes; critical dimensions of behavioral expression that confer risk such as emotion regulation, and impulse control and executive functions.

**Adult Psychopathology and Prevention Research Branch.** This branch focuses on research that reflects significant public health concerns. These include: identifying prevalence and risk factors for mental disorders across the life span, developing new approaches to the etiology and assessment of adult psychopathology and related impairment, and translating the findings and methods of basic research into studies of the

biobehavioral mechanisms of disorders and the development of new preventive, treatment, and rehabilitative interventions.

### **Health and Behavioral Science Research Branch.**

This branch supports research on general medical illnesses and behavior and their relationship to mental disorders. Emphasis is on the mechanisms and processes linking medical and mental illnesses, development and testing of early interventions, factors that influence adherence to treatment, help seeking behavior, cognitive and decision making factors that influence the choice of treatment or mental health services, stigma and services utilization.

All applications relevant to the mission of the Division of Mental Disorders, Behavior and AIDS will receive full consideration. Possible areas for future research include:

- A. **Instrumentation for Basic, and Clinical Behavioral Research.** Modern equipment that uses the most recent technological advances is needed so that mental disease can be related to dysfunction(s) of the CNS. Once these dysfunctions are identified and localized, rational therapies can be developed and evaluated.
  1. **Physiological Monitoring.** Techniques and equipment for continuous monitoring of physiological data (e.g., temperature, activity, sleep duration, EEG activity, ECG, pulse rate). Computer programs that can record, catalog, categorize and identify interrelationships between several of the above measures. Appropriate areas for behavioral clinical research would include developing:
    - a. Reliable non-invasive means of chronic monitoring of physical activity and physiological measures such as body temperature.
    - b. Software and hardware analyzing and providing experimental control over multiple single unit recordings, on-line and in real time.
  2. **Measurements of Infant Development Using Physiological and Behavioral Measures.**
    - a. Psychophysiological measures to evaluate infants during the first six months of life.



- b. Miniaturized non-invasive instruments to record psychophysiological data (e.g., heart and respiration rate, galvanic skin response, and defensive motor behavior).
- c. Telemetry capability for non-invasive devices so that infants can be monitored for prolonged periods without interfering with their behavior.
- d. Computer programs and inexpensive computers that will collect, analyze and identify recurring patterns in the psycho-physiological measure(s) of interest.

3. **Behavior Monitoring and Analysis.**

- a. Improve or create new video devices to monitor animal and human behavior and ease analysis of behavior.
- b. Computer software to ease analysis of behavior monitored by video or telemetry systems.

B. **Behavioral Science, Research and Development.**

It is important to develop reliable methods that can correctly identify the normal and abnormal components of cognitive, emotional, and psychosocial behavior in human development. Computer-based methods of accomplishing this are also needed to increase the accessibility and reliability of information made available to the research community.

1. **Assessment Tools.**

- a. New technologies to assess and validate occurrence of and injuries resulting from physical and sexual abuse.
- b. Technologies to assess CNS effects of psychosocial variables and interventions.
- c. Innovative approaches to assessing mental disorders using new statistical and psychometric techniques such as Item Response Theory.

2. **Methodological Research and Development.**

There is a need to devise new ways of data collection, analysis, management and dissemination.

- a. New relatively culture-free taxonomies and/or measures of basic behavioral and social phenomena that can be

employed in research across socio-cultural contexts.

- b. Innovative computer-based observation techniques, and computer software and hardware that allow on-line methods for characterization of interpersonal interactions in groups.
- c. Low cost microcomputer software for the recording and analysis of patterns and sequences in observed social interactions.
- d. Causal modeling methodology as applied to correlational longitudinal data sets.
- e. A data translation and communication package for collecting, archiving, and making available existing longitudinal behavioral sets to the scientific community for secondary or meta-analyses.
- f. Flexible user-friendly software for control of timed, multi-modal stimulus presentation and response collection for experiments on perception and cognition.
- g. Development of improved standardized instruments and methods for assessing assets, deficits, and disorders in children's social and emotional functioning that are sensitive to variations in social-environmental contexts.
- h. Innovative methodologies for assessing continuity and change in neighborhood/community context variables.
- i. Innovative methodologies for assessing and integrating historical neighborhood/community contextual variables with existing data sets.

C. **Health and Behavior and Prevention.**

- 1. Innovative, computer-based methods to monitor prevention and intervention efforts and correlate them with outcome measures are needed. Results should be accessible to other interested parties without compromising the privacy of the individual. Evaluations could allow a multivariate analysis of relationships among the following:

- a. Perceptual, personality, cognitive and neuro-psychobiological test data.
- b. Verbal-linguistic characteristics.
- c. Motor behavior and facial responses.
2. Development of innovative programs and methodologies aimed at mental disorder prevention and mental health promotion, including regular and interactive video models, especially those appropriate to minority populations.
3. Develop technologies that improve adherence in interventions aimed at mental disorders, for example, innovative telephone reminder systems or interactive Internet programs.
4. Development of new programs, materials and technical approaches to encourage the adoption by health practitioners of innovative efforts to improve adherence to medical and lifestyle regimens.
5. Development of innovative approaches to assist health care practitioners in dealing with problems of family violence including abusive injuries to children.

D. **Science Education in Mental Disorders, Behavior and AIDS.** There is a critical need for improvement in science education, particularly in areas specifically related to brain, behavior and mental illness.

1. Research on the best ways to present neuroscience and behavioral science information to particular groups of students (e.g., kindergarten through sixth grade; African Americans, Hispanics, persons with physical and cognitive disabilities).
2. Computer-based systems to teach students how to observe scientific phenomena related to the brain, behavior and mental illness, and to report them clearly in writing.
3. Research on better ways to communicate new knowledge and directions of scientific growth in the area of neuroscience and mental illness to teachers and curriculum developers.
4. Development of new approaches to reduce stigma and the frequent misperceptions that accompany stigmatized views regarding mental illness.

E. **Diagnosis and Assessment of Emotional and Psychological States.**

1. Automated methods to detect specific emotional states using behavioral and autonomic indicators.
2. Development of techniques for maintaining or restoring mental capacities in older adults who experience declining learning and memory abilities due to age-related brain disorders.
3. Development of behavioral and laboratory measures to define and assess specific impairment-related components of psychiatric disorders, e.g., cognitive dysfunctions in schizophrenia.
4. Development of standardized and valid instruments to assess exposure to traumatic events and victimization experiences as well as the physical and mental health consequences of such exposure.
5. Develop measures that quickly, reliably and validly assess co-morbid mental and physical disorders in primary care and specialty medical settings.

F. **Knowledge Transfer.**

1. Computerized, Internet-based data storage, analysis, and retrieval systems to provide professionals and the general public with current information on mental disorders and behavioral dysfunctions and their prevention and treatment.
2. Systematic approaches to the dissemination of the latest clinically-relevant NIMH-supported research findings to relevant populations of service providers, advocacy groups, client groups, and policy makers, e.g., by means of targeted research summaries, recruited list serves, or other print or electronic communication.

**NIMH Center for Mental Health Research on AIDS**

The NIMH office on AIDS Research supports research on the effects of HIV on the central nervous system and on developing effective HIV prevention and risk reduction interventions. In addition to the topics listed below, the Center welcomes a wide range of applications dealing with HIV/AIDS prevention issues. Inquiries are

encouraged. Examples of possible SBIR initiatives include:

A. **Behavior Change and Prevention Strategies.**

To reduce HIV transmission especially among minority populations and hard to reach subsets of those populations.

1. Development of methods to reduce, prevent and/or change HIV-associated and STD risk behaviors.
2. Development of relapse prevention methods for HIV-associated risk behaviors.
3. Development of curricula for training clinicians and other health care practitioners in the prevention and treatment of HIV-related mental disorders.
4. Development of school-based curricula to promote HIV prevention by educators and teachers.
5. Development of HIV prevention materials to be used in community-based outreach programs for special populations (school dropouts, homeless, street youth, incarcerated youth).
6. Development of curricula for training in multicultural issues and development of cultural competence in HIV risk assessment, counseling, and prevention.
7. Development of print and/or computer based materials to assist primary care practitioners in informing their patients about HIV risk and prevention.
8. Development of innovative approaches to reduce stigma often expressed toward individuals with HIV/AIDS.
9. Development of materials and other programs to assist health care practitioners in improving patient adherence to medical and lifestyle regimens.

B. **Neuro-AIDS: HIV-1 Infection and the Nervous System.**

1. Development of novel non-invasive (e.g., neuroimaging) approaches to assess and study mechanisms of neurologic and neurocognitive dysfunction associated with HIV infection.
2. Development of in-vivo and in-vitro models to assess mechanisms of HIV-1 trafficking into and out of the CNS, mechanisms of

neuropathogenesis and therapeutic strategies for eradicating HIV-1 in the CNS.

3. Development of novel molecular markers that are correlated with HIV associated with dementia.
4. Development of novel molecular approaches to study compartmentalized viral evolution in the CNS.
5. Development of improved anti-retroviral therapeutic strategies for targeting CNS infections including: facilitated entry of anti-retroviral therapeutic agents through the blood-brain barrier by manipulation of transporter systems and development of novel anti-retroviral therapeutic agents that readily pass through the blood-brain barrier.
6. Development of novel therapeutic approaches to block or reverse CNS dysfunction associated with HIV infection.

C. **AIDS Mental Health Services Delivery.**

1. Video and computer-assisted methods to train health and mental health care providers in the psychosocial and neuropsychiatric aspects of HIV infection and AIDS.
2. Development of methods to assess functioning in families in which there is an HIV infection in order to develop improved treatment modalities.
3. Development of novel programs to train people infected with HIV in self-care management and identification of stress and development of improved coping strategies in order to improve quality of life.
4. Development of novel programs to help people recognize and seek treatment of mental health problems arising from living with HIV/AIDS as a long-term chronic condition.
5. Development of information, instruments or methodologies to improve and/or track adherence to complex HIV/AIDS drug therapies for Hispanic and African American populations.
6. Development of innovative approaches to link researchers with community providers in the implementation of research-based HIV prevention efforts at the community level.

For further information on mental disorders, behavior, or AIDS research topics, contact:

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### **Division of Services and Intervention Research**

The Division of Services and Interventions Research supports research, research demonstrations, research training, resource development, and research dissemination in prevention and treatment interventions, services research, clinical epidemiology, and diagnostic and disability assessment. The division is comprised of three branches: Services Research and Clinical Epidemiology Branch, Adult and Geriatric Treatment and Preventive Intervention Research Branch, and Child and Adolescent Treatment and Preventive Intervention Research Branch.

#### **Clinical Trials, Clinical Practice, and Effectiveness Research.**

This division is concerned with both the translation of neuroscience and behavioral science knowledge into clinical practice and with the development of research on the effectiveness of treatment and rehabilitation. This involves clinical and clinical services research on the delivery of mental health services in hospitals, clinics, communities, and in a wide variety of systems of care, e.g., managed care, primary care, etc.

#### **A. Services Research and Clinical Epidemiology Branch.**

The branch supports research on the organization, financing, delivery, effectiveness, and appropriateness of mental health care in everyday settings in order to find ways to improve the effectiveness, efficiency, and equity of mental health services (including preventive services) in community and other settings. Also supported are studies on pharmacoeconomics, pharmaco-epidemiology, and the distribution, determinants, and course of mental illness in the context of various clinical settings. Mental health services include mental health care provided in specialty mental health and general health care settings, including primary care, hospitals, nursing homes, and other residential care settings, as well as in educational settings

and various legal system settings, such as jails, juvenile detention and correctional facilities, prisons, and probation and parole programs. Other services often needed by mentally ill persons include social services, vocational and rehabilitation services, welfare, and housing. Relevant services include those provided to children and adolescents with emotional disorders, adults and elderly adults with mental disorders, and persons with mental illness that co-occurs with physical illness and with alcohol and/or drug abuse disorder. Research methodologies include ethnographic studies, surveys, and analyses of secondary data, randomized controlled trials, quasi-experimental designs, cohort, and case-control studies.

Advances in clinical epidemiology, mental health treatment and services research fields have made it imperative that intensive work continue in the areas of assessment/screening technologies, outcome assessment measurement and measurement packages, dissemination technologies, data analysis techniques, and the training of clinicians and providers. The translation of efficacious and effective treatments into primary care, community mental health centers, and managed care settings is both a major challenge and opportunity to develop technologies and systems that will improve the care and rehabilitation of patients and enable them to profit from the research advances that have been made. Research is needed on the dissemination of empirically supported treatments or services.

#### **1. Methodological Research Program.**

Development, testing, and refinement of methodologies and instruments to facilitate research on services for mentally ill persons, including measures of severity of illness, family burden, social support, quality of care, effectiveness of care, direct and indirect cost of mental disorders, and short-term and long-term outcome measures; studies submitted by statisticians, psychometricians, and other experts in research methodology and scientific data analysis for work on the design, measurement, and statistical challenges inherent in conducting mental health services research.

#### **2. Outcomes and Quality of Care Research.**

Tools, scales, and measures to assess

differences in quality and outcomes of care in various practice types and tools to monitor outcome and quality; analyze the appropriateness of treatment including medications; development of tools and methods to assess the coordination of treatment and other care across settings and over periods of time.

3. *Managed Care and Systems Research.*

This program supports studies on the organization and delivery of mental health services and related services in different settings. Methods and tools are needed: to evaluate the impact of various processes of managed behavioral health care, such as utilization management, gatekeeping, and case management on access, cost, and quality; the analysis of managed care structures across sectors which promote linkage and integration between different providers; to examine ways to coordinate mental health, health, and human service systems financed by public and/or private resources to provide cost-effective care.

4. *Sociocultural Research Program.* This program is concerned with strengthening the theoretical and empirical base for mental health services research by including approaches that derive from sociology, anthropology, and the behavioral sciences in general. The program supports research relating to issues of culture, social systems, and social networks as they relate to help seeking, use, and provision of services, effectiveness, quality, and outcomes of services. Methods and tools are needed to assess need for clinical services, effective ways of providing culturally competent care, and assessing outcomes for persons from differing social and cultural groups.

5. *Child and Adolescent Services Research Program.* This program includes research on patterns of mental health service use, and the quality, organization, and financing of services for children with mental disorders and their families; services provided in multiple sectors and settings, such as schools, primary care, child welfare, juvenile justice, and mental health; service needs and delivery of services to subpopulations of youth with co-morbidities of various types; clinical and economic evaluation of innovative service models.

Methods and tools to address the above areas are needed.

6. *Cost and Financing Research.* This program includes research on economic factors affecting the delivery of mental health services including the economic burden of mental illness; financing and reimbursement of public and private mental health services; impacts of alternative financing methods such as capitation, risk-adjusted contracting, and physician fee schedules on the cost of mental health care; pharmacoeconomics; evaluation of insurance coverage and various benefit designs including mandated coverage and mental health insurance parity; cost benefit, cost-effectiveness, and cost-utility analysis of mental health service interventions; market forces affecting demand for and supply of mental health care; and economic analysis of practice patterns of different mental health providers. The development of effective ways to access and use fiscal and outcome data that is often private or unavailable for research is needed. Also, statistical and methodological tools, computer software, and other analytic approaches to address the above issues, such as cost benefit, and cost-effectiveness analyses.

7. *Primary Care Research.* This program includes studies on the delivery and effectiveness of mental health services within the general health care sector; recognition, diagnosis, management and treatment of mental and emotional problems by primary care providers; coordination of general medical care with and referrals to mental health specialists; provision of psychiatric emergency services, consultation/ liaison psychiatry, and other psychiatry, psychology, and social work services within the general medical care sector; studies which improve understanding of how best to assess mental disorders and provide mental health services in general health care settings. Methods and tools to study this area at the patient, provider and organizational level are needed.

8. *Clinical Epidemiology Research.* This program includes epidemiologic studies of mental disorders in clinical settings, including studies dealing with clinical

decision-making in personal-encounter care for individual patients; studies concerned with the procedures and standards needed for scientifically rigorous studies of complex clinical phenomena that occur in patients; pharmacoepidemiology studies; research to identify risk factors for the development of mental disorders in clinical settings; factors important in the natural history of mental disorders, including co-morbid conditions, and the rates of occurrence of mental disorders in clinical populations. Methods to study decision-making, to more efficiently and accurately assess disorders and levels of functioning, and to study the interaction of patients and clinicians in various settings are needed.

9. **Diagnosis and Disability Assessment Research.** This program includes research that develops and evaluates standardized methods for measuring and classifying psychiatric disorders and their disablements; studies the validity and boundaries of diagnostic categories and disablement assessments; develops computer software relevant to the diagnosis, classification, and study of psychiatric disorders and their disablements; studies of the frequency of psychiatric disorders and their associated disablements in clinical settings, and in general and special community groups. Methods to reliably and accurately assess psychiatric disorder and disability in clinical settings are needed.

- B. **Adult and Geriatric Treatment and Preventive Interventions Research Branch.** The focus is on the treatment, prevention, and rehabilitation of mental disorders in adults, including older persons. The focus is broad and inclusive with respect to the heterogeneity of patients, the severity and chronicity of disorders, the variety of community and institutional settings in which treatment is provided, and the range of outcomes measured. Disorders studied include: all mental disorders; Alzheimer's disease and related dementias; suicide; eating disorders, sleep disorders; and disorders related to the menstrual cycle. Interventions studied include pharmacologic approaches (individual drugs and combinations of drugs), somatic approaches (e.g., electroconvulsive therapy),

behavioral and psychotherapeutic approaches (e.g., cognitive therapy). Research is supported on individual and combined approaches; time frame includes acute, continuation, and maintenance studies and long-term symptomatic management and improvement of functional status.

Human subjects include adult and geriatric age groups covering the full range of mental disorders individually and in complex patterns of comorbidity with other mental disorders (e.g., anxiety + depression), substance abuse (e.g., depression + alcohol abuse), brain disease (e.g., stroke + depression), or physical illnesses (e.g., sensory impairment + psychosis). Normal controls are often used in studies. Settings of research include academic or non-academic specialty services (psychiatry, neurology, etc.), primary care settings, hospitals, nursing homes, outpatient clinics, and home health under managed care or fee-for-service. Other settings for research include occupational health programs, community centers, and correctional facilities. Research must include active interventions for mental disorders and behavioral dysfunctions; observational studies are assigned elsewhere. Areas supported are: trials to establish the short- and long-term efficacy of interventions; studies that assess the effectiveness/cost effectiveness of interventions in standard or usual practice settings; off-label or innovative applications of established treatments; comparative studies of alternative treatments; clinical pharmacokinetic/pharmacodynamic studies; strategies for augmentation/combination and for reduction/taper; correlates of treatment response/basis for treatment failure with established agents; studies designed to develop and refine methodology for use in intervention research; and treatment algorithms/strategies for improvement of clinical care.

1. **Somatic Treatments Program.** Areas include electroconvulsive therapy (ECT), repeated transcranial magnetic stimulation (RTMS), bright light, physical exercise, and similar approaches in all areas of Branch program support.
2. **Adult Psychopharmacology and Geriatric Psychopharmacology Programs.** Areas include clinical psychopharmacology (Phase 3 and 4 type studies), new/innovative applications for established



treatments, studies of side effects and adverse reactions to pharmacologic treatment (tardive dyskinesia, cognitive impairment etc.), new approaches to dosing (e.g., in geriatric patients), treatment duration and intensity, and tapering/cessation/withdrawal strategies in all areas of program support.

3. **Adult Psychotherapy and Geriatric Psychotherapy Programs.** Application of new psychotherapeutic, behavioral, and psychosocial treatments, assessment of standardized approaches to treatment (based on treatment manuals), and innovative applications of new treatments in all areas of program support.
4. **Combined Treatments Program.** All research that combines different treatment modalities in a single combined or comparative protocol (e.g., pharmacologic plus psychosocial intervention). Multiple approaches within the same class of modalities (e.g., two drugs or two psychotherapies) would not be considered combined treatment for programmatic purposes.
5. **Preventive Interventions Program.** Preventive intervention studies, including those designed to reduce the occurrence of mental disorders, dysfunctions and related problems within asymptomatic and subclinical populations and those related to treatment (e.g., prevention of relapse, recurrence, inappropriate resource use) or side effects (prevention/minimization of tardive dyskinesia, etc.). A specially designated programmatic focus is in the area of suicide prevention.
6. **Rehabilitative Interventions.** Rehabilitative interventions related to optimizing long-term outcomes of treatment with respect to function, disability, and quality of life.

C. **Child and Adolescent Treatment and**

**Preventive Intervention Research Branch.**

The branch supports research focusing on the treatment, prevention, and rehabilitation of mental disorders in children and adolescents. The focus is broad and inclusive with respect to the heterogeneity of patients, the severity and chronicity of disorders, the variety of community and institutional settings in which treatment is provided and the range of outcomes measured. Disorders studied include all mental and

behavioral disorders. Interventions studied include pharmacologic approaches (individual and combination medications), somatic approaches, behavioral and psychotherapeutic approaches. Research is supported on individual and combined approaches, time-frame includes acute, continuation, and maintenance studies and long-term symptomatic management and improvement of functional status.

Human subjects include child and adolescent age groups covering the full range of mental disorders individually and in complex patterns of comorbidity with other mental disorders and behavioral problems (e.g., anxiety and depression), substance abuse (e.g., depression and alcohol abuse), brain disease or physical illnesses. Normal controls are often used in studies. Settings of research include academic or non-academic services (child psychiatry, neurology, etc.), primary care settings (e.g., pediatrics), hospitals, group homes, foster care, schools, and outpatient clinics under managed care or fee-for-service. Other settings include community centers, group homes and juvenile justice facilities. Research must include active interventions for mental disorders and behavioral dysfunctions; observational studies are assigned elsewhere. Areas supported are: trials to establish the short- and long-term efficacy of interventions; studies that assess the effectiveness/cost effectiveness of interventions in standard or usual practice settings; off-label or innovative applications of established interventions; comparative studies of alternative interventions; clinical pharmacokinetic/pharmacodynamic studies; strategies for augmentation/ combination and for reduction/taper; correlates of treatment response/basis for treatment failure with established agents; treatment algorithms/strategies for improvement of clinical care; and studies designed to develop and refine methodology for use in intervention research.

1. **Pharmacologic Treatment Intervention Program.** Areas include clinical psychopharmacology (Phase 3 and 4 type studies), new/innovative applications for established treatments, studies of side effects and adverse reactions to pharmacologic treatment (e.g., tardive dyskinesia, etc.), tapering/cessation/

withdrawal strategies and somatic treatments in all areas of program support.

2. ***Combined Intervention Program.*** Areas include all research that combines different treatment modalities in a single combined or comparative protocol (e.g., pharmacologic plus psychosocial intervention). Multiple approaches within the same class of modalities (e.g., two medications or two psychotherapies) would not be considered combined treatment for programmatic purposes.
3. ***Psychosocial Intervention Program.*** Areas include development and application of new psychotherapeutic, behavioral, and psychosocial treatments, assessment of standardized approaches to treatment (based on treatment manuals), and innovative applications of new treatments in all areas of program support.
4. ***Preventive Intervention Program.*** Areas include all preventive intervention studies, including those designed to reduce the occurrence of mental disorders, dysfunctions and related problems within asymptomatic and subclinical populations and those related to treatment (e.g., prevention of relapse, recurrence, inappropriate resource use) or side effects (prevention/ minimization of tardive dyskinesia, etc.). A specially designated programmatic focus is in the area of suicide prevention.

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#### **NATIONAL INSTITUTE OF NEUROLOGICAL DISORDERS AND STROKE (NINDS)**

The mission of NINDS is to reduce the burden of neurological disease—a burden borne by every age group, by every segment of society, by people all over the world. To this end, the Institute supports and conducts research on the healthy and diseased brain, spinal cord, and peripheral nerves. Hundreds of disorders afflict the nervous system. Common killers and disablers such as Parkinson's disease, Alzheimer's disease, multiple sclerosis, stroke, epilepsy, and autism are well known. Other disorders we study may be known only to the patients and families affected, their doctors, and scientists who look to rare disorders for help in understanding the brain as well as treating more common diseases.

Examples of research topics within the mission of the NINDS that may be of interest to small businesses are shown below. For additional information about areas of interest to the NINDS, please visit our home page at <http://www.ninds.nih.gov>.

Extramural research is organized in the following programmatic areas within NINDS: neurodevelopment, neurogenetics, repair and plasticity, systems and cognitive neuroscience, channels, synapses and circuits, neurodegeneration, neural environment, and technology development. Specific areas of interest are listed below:

## Neurodevelopment

- A. Development of computer software to permit reconstruction of magnetic resonance imaging (MRI) from unrestrained patients or animals that may change position within the MRI magnetic field.
- B. Development of technology to assess fetal neurological integrity such as fetal MEG.
- C. Non-invasive monitoring of brain function such as improvements in PET imaging, MRI imaging and spectroscopy, and methods of optical imaging such as development of near infrared spectroscopy (NIRS) for monitoring of changes in cerebral oxygen saturation, cerebral blood flow and volume, and oxygen utilization in the brain, and for functional imaging utilizing scattering and absorption characteristics of brain tissue.
- D. Non-invasive techniques for structural imaging, such as near infrared imaging.
- E. Development of computerized histological tomographic brain atlas graphics, which can be stored and manipulated on a personal computer for teaching, research data modeling and display, and correlation with clinical neuroimaging.
- F. Development of practical imaging modalities in extremely ill very low birth weight infants.
- G. Non-invasive techniques for assessment and continuous bedside monitoring of cerebral function in the neonate, such as, but not limited to, functional near infrared spectroscopy and amplitude-integrated EEG.
- H. Development of improved technology for MRI imaging of infants and small children, for example, specially designed pediatric sized head coils, or devices to minimize movement artifact in unsedated infants.

## Neurogenetics

- A. Analysis of central nervous system cell lineages for treatment of neurodevelopment and degenerative disorders.
- B. Development of embryonic stem cell models of nervous system development and function.
- C. Development of technology for the production of high quality cDNA libraries from small tissue samples of the brain during development and in

response to disease, injury or pharmacological agents.

- D. Identification of optimal DNA vector systems to standardize and expedite the sequencing of cDNA libraries derived from micro dissected brain tissues.
- E. Development of technology for micro dissection of brain tissue for single cell analysis of gene expression.
- F. Development of informatics systems to expedite the analysis and use of sequence data that will be derived from projects to identify novel genes and to map temporal and spatial dimensions of gene expression in the brain.

## Repair and Plasticity

- A. Neural Prostheses and Deep Brain Stimulation.
  1. Design, development, and evaluation of neural recording and stimulating microelectrodes for neural prostheses and deep brain stimulation.
  2. Development of thin, insulating coatings to make implanted electronic packages impervious to the corrosive action of body fluids and tissues.
  3. Development of transducers of position, touch, and force for use in functional electrical stimulation systems.
  4. Development of electrodes for sensing specific neurotransmitters.
  5. Non-invasive methods of focally stimulating small populations of neurons within the body.
  6. Development of communication aids for individuals with "locked-in syndrome."
  7. Development of a complete system utilizing existing microelectrodes, lead wires and percutaneous connectors to transfer neural signals outside the body.
  8. Develop new high charge density electrode materials.
  9. Development of a method to repeatedly inhibit neuronal electrical activity in a safe and effective manner.
  10. Development of a non-invasive method of selectively stimulating and/or inhibiting small groups of nerve fibers within a nerve trunk.

11. Development of materials to minimize scarring following surgery in the central nervous system.
12. Development of techniques for precise functional placement of microelectrodes within the central nervous system.
13. Neural control of micturition and defecation for individuals with spinal cord lesions.

B. CNS Trauma and Rehabilitation.

1. Development, testing, and evaluation of devices, methods, or drugs to aid the neurologically injured.
2. Means of assisting or achieving restitution of function in victims of injury to the nervous system.
3. Develop transgenic, knockout and inducible knockout animal models for stroke and CNS trauma research.
4. Develop technology for data gathering and analysis for assessment of multiple parameters of ICU recording in brain trauma.
5. Develop instruments or techniques to enhance monitoring of nervous system activity during surgical procedures, aimed at improving the safety, targeting or efficacy of those procedures.
6. Develop reporting instruments for data collection and analysis in clinical studies of head injury.
7. Develop a novel means of preclinical testing for new and promising therapies for acute and chronic central nervous system injury.
8. Development of a simplified registry and follow-up technique for patients with brain and spinal cord injury.
9. Development of monitors for such modalities as intracranial pressure, brain temperature, and cerebral blood flow.
10. Development of consortia to share data on head injury patients, design clinical protocols, and conduct clinical trials in traumatic brain injury.
11. Establishment of networks to test pharmaceutical agents in animal models of CNS trauma.

12. Develop drugs or other agents to reduce scarring after spinal cord injury.
13. Develop and test novel biological assays for use as diagnostics in acute stroke (ischemic vs. hemorrhagic), traumatic brain injury, and spinal cord injury.

C. Neuroimaging.

1. Development of ultrasound imaging methods for the central nervous system.
2. Development of functional imaging techniques.
3. Development of imaging techniques to track the course of injury and repair following spinal cord injury.
4. Development of imaging techniques for image guided surgery in the CNS.

D. Stem Cell Biology.

1. Development of a website and database for posting and discussion of protocols used in harvesting, maintaining in culture, and inducing differentiation of neural stem cells.
2. Development of a stem cell repository for the storage of stem cells from different sources and immortalized cell lines, and for making these reagents readily available to the research community.
3. Develop efficient and reproducible methods for harvesting and storing stem cells for research use.
4. Develop methods for the delivery of growth factors, cells, genes and other agents to specific sites within the nervous system.
5. Develop markers for the identification and/or harvesting of stem and progenitor cells in the nervous system and in non-neural tissues.
6. Develop methods for phenotyping stem and progenitor cells in the nervous system.
7. Use of mutant and transgenic mice or rats to study the effect of identified genetic alterations on neurogenesis in the adult central nervous system.
8. Develop methods and reagents that would allow tracking of grafted cells in the living host animal using non-invasive imaging methodologies

E. *Axonal Regeneration/Guidance and Synapse Formation.*

1. Develop biomaterials to serve as paths for supporting or guiding axonal growth across a site of injury.
2. Develop methods to deliver neurotrophic factors, cells or genes to injured brain sites to enhance regeneration or restoration of function.
3. Develop biomaterials to promote sprouting and directed growth of axons toward specific sites in the central nervous system.
4. Develop biomaterials to promote dendritic growth and stability, and synapse formation in localized areas.

## **Systems and Cognitive Neuroscience**

A. *Cognitive and Behavioral Neuroscience.*

1. Development of computerized neuropsychological assessment tools to facilitate testing of neurologically impaired subjects.
2. Development of techniques and devices for imaging of small animals such as transgenic and knockout animal models of complex behaviors.
3. Design, development, and evaluation of automated systems for assessment of behavioral parameters.
4. Development of computer software that integrates imaging and physiological measures of brain activation.

B. *Sleep Neuroscience.*

1. New therapies for sleep disorders.
2. New methods for quantifying optimal alertness.
3. Models of neurological sleep disorders.
4. Novel applications of evoked potentials to sleep neuroscience.
5. Further development of portable devices that facilitate cost-effective screening for potential sleep disorders, and can be used to monitor the progress of already diagnosed sleep disorders.

C. *Pain.*

1. Development of objective methods for quantitative assessment of pain, including development of a quantitative sensory testing battery for pain patients.
2. Development of novel pain model systems, particularly more accurate pre-clinical experimental models.
3. Development of tools to elucidate potential analgesic targets, and models for testing and validating these for efficacy in patients.
4. Development of new diagnostic tools for different pain mechanisms and objective measures of analgesic drug action.

D. *Neuroimaging.*

1. Development of devices for artifact-free monitoring of vital neurological parameters during MRI procedures involving very high static and dynamic magnetic fields (greater than 2 Tesla) and high-energy microwave radiation typical of the MRI environment.
2. Development of functional imaging techniques.
3. Development of combined imaging strategies, i.e., fMRI and PET.

## **Channels, Synapses and Circuits**

A. *Epilepsy.*

1. Devices for automated detection and quantification of seizures.
2. New therapies both for the control of seizures and for the prevention of the development of epilepsy.
3. New formulations and delivery systems for antiepileptic drugs.
4. New models of seizures and epilepsy useful for screening therapies.
5. Improved methods of monitoring compliance/medication dispensing.

## **Neurodegeneration**

- A. Development and preliminary testing of instruments, devices, or drugs that enhance diagnostic, treatment, or monitoring capabilities.
- B. Identification or development of animal models for research on neurodegenerative disorders.

- C. Development of early or presymptomatic diagnostic procedures for neurodegenerative disorders.
- D. Epidemiology of neurodegenerative disorders.
- E. Development of an ambulatory monitor to measure fluctuations of movements in patients with degenerative neurological disorders.
- F. New delivery methods of medications for degenerative neurological disorders.
- G. Development of cell lines for in vitro modeling of neurodegenerative disorders.
- H. Therapeutic drug discovery targeted to neurodegenerative disorders.
- I. Development of drug screening assays, including biochemical, cellular or model organism assays for high-throughput screening approaches.

## Neural Environment

### A. Infectious and Immune Disorders.

1. Development of therapies to prevent, arrest or reverse autoimmune neurological disorders such as multiple sclerosis.
2. Development of methods that aid the diagnostic of infectious and immune disorders.
3. Development of methods or vectors for the delivery of biologics (e.g., cytokines, DNA), drugs, and other agents to the nervous system.
4. Development and studies of drugs with high blood brain barrier permeability intended for treatment of CNS infections including HIV-related opportunistic infections.
5. Development of animal models for infectious and immune disorders (e.g., k.o. or transgenic mice, viral systems) that allow the study and identification of the effect and contribution of genes to disease.
6. Development of techniques such as microarray, gene expression analysis or immunological techniques that allow the study and identification of the effect and contribution of genes to disease or the effect of therapies.
7. Development of techniques such as microarray, gene expression analysis or

immunological techniques that allow studies on the mechanisms and effect of therapies.

8. Development of functional and other imaging techniques and tools, and of combinations thereof.

### B. Stroke.

1. Development, testing, and evaluation of devices, methods, or drugs to aid in the prevention, diagnosis and treatment of stroke patients.
2. Mass spectrometry for the analysis of protein expression in the ischemic CNS.
3. Develop and validate large and small animal models, including transgenic, knockout, and inducible knockout animal resources, that reflect the complexity and diversity of the human brain and its response during stroke.
4. Brain specific gene and protein transfer methods for delivery to cerebral vessels, neurons, or glia in the ischemic CNS.
5. Methods and devices for high throughput genomic and proteomic expression and data analysis in stroke.
6. Methods to transiently suppress gene and protein expression in brain ischemia.
7. Expand brain imaging capabilities to include new methods of imaging, synthesis of radiolabeled ligands for specific receptors, and refinement of functional, structural and metabolic imaging techniques.
8. Improve databases for stroke to include sharing of clinical descriptions, genomic or proteomic data, or tracking of the availability of tissue specimens from existing brain banks.
9. Surrogate markers for neurodegenerative, vascular, and immune diseases of the brain.

### C. Brain Tumors.

1. Development, testing, and evaluation of devices, methods, or drugs to aid in the prevention, diagnosis and treatment of CNS tumors.
2. Advancement of molecular analysis of DNA, RNA and protein in CNS tumors.



3. Surrogate markers for cerebrovascular, immune, and infectious diseases and CNS tumors.
4. Develop methods for identification of specific neural cell lineages.
5. Techniques for brain specific antisense, gene and protein transfer into cerebrovascular, neurons, or glial cells in brain tumors.
6. Methods to deliver brain specific proteins and genes through the blood-brain and blood-CSF barriers for targeting CNS tumors.
7. Mass spectrometry for the analysis of protein in the CNS and in brain tumors.
8. Highly specific radiolabeled markers for different types of brain tumors that can be used under histopathological or brain imaging conditions.
9. Development of an intracranial pressure monitor.
10. Refinement of functional, structural and metabolic imaging techniques for brain tumors.
11. Methods and devices for high throughput genomic and proteomic expression and data analysis in brain tumor.

D. Prion Diseases.

1. Development of a rapid and sensitive assay for the detection of normal and variant prions as well as the detection and isolation of various prion strains.
2. Transgenic, knockout and inducible knockout animal resources for Transmissible Spongiform Encephalopathy research.

### Technology Development

- A. Animal models, including genetic and experimental models of neurological disorders; examples include mouse mutants, models of spinal cord injury or traumatic brain injury, epilepsy, and channelopathies.
- B. Neuroinformatics, including relational software for genetic, functional, and anatomical data; databases; and websites for data sharing.

- C. Computational tools for understanding both cellular and systems level function in the nervous system.
- D. Approaches to recording and stimulating neural activity, including single cells, cellular ensembles, and brain regions or fiber tracts.
- E. Imaging tools, including MRI, fMRI, MRS, PET, MEG, optical and infrared, and ultrasound, both for human and animal studies.
- F. Approaches to identify and characterize genes involved in function and pathology in the nervous system, including microarrays, genetic linkage methods, mutagenesis, expression analysis, and in situ localization.
- G. Approaches to identify and characterize proteins involved in function and pathology in the nervous system, including electrophoretic, immunochemical, and mass spectrometric analyses.
- H. Therapeutic drug discovery, including the development of molecular, cellular, or animal-behavioral screening assays; high-throughput screening approaches; and preparation of drug candidate chemicals or chemical libraries by traditional or combinatorial chemical approaches.
- I. Bioengineering, including neural prostheses.

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**NATIONAL INSTITUTE OF NURSING RESEARCH (NINR)**

The NINR supports research focused on biological and behavioral aspects of critical health problems that confront the Nation. Emphasis is on seeking ways to reduce the burden of illness and disability by understanding and easing the effects of acute and chronic illness, improving health-related quality of life by preventing or delaying the onset of disease or slowing its progression, establishing better approaches to promote health and prevent disease, and improving clinical environments by testing interventions that influence patient health outcomes and reduce costs and demand for care.

For additional information about areas of interest to the NINR, please visit our home page at <http://www.nih.gov/ninr/>.

**Research and Development of Technologies that Promote Alleviation, Adaptation, or Management of Symptoms**

- A. Technologies to be used in the hospital, long-term care, hospice, or home setting to validate clinicians/patients' assessment of chronic problems such as congestive heart failure, cystic fibrosis, organ failure, dementia, renal disease, and asthma.
- B. Devices to improve delivery of nursing care for patients who have restricted or impaired movement due to conditions such as spinal cord injury, intractable pain, life sustaining equipment such as dialysis machines and left ventricular assist devices, or orthopedic fixation devices.
- C. Devices to assist teenagers to quit smoking.
- D. Devices to improve peak flow use for children with asthma in the home and at school.
- E. Devices to diagnose and screen for COPD early in the course of the disease, particularly targeting young adults.
- F. Devices to assist in providing palliative care for patients through the disease trajectory and at the end of life.

### Research and Development of Technologies to Enhance Self Care and Clinical Care

- A. Technologies to assist patients to adhere to chronic regimens such as reminding children to take steroid inhalers during the day for asthma; alerting obese adults when high calorie and fat content foods are about to be eaten; and prompting sedentary adults to exercise.
- B. Telehealth technologies to improve delivery of patient care such as assessing injury severity or traumatic injury in children and adults and transmitting this information to acute care settings for assessment and evaluation; and communicating signs and symptoms of clients at home to health care providers in distant locations; and tailoring nursing care for diverse patients in a wide variety of settings.
- C. Technologies to treat chronic wounds that fail to heal, specifically decubitus ulcers, venous stasis ulcers, and diabetic ulcers.
- D. Technologies to be used in the hospital or home care setting to monitor or assess preterm infants.
- E. Technologies to assist informal caregivers in providing care or assistance to family members in the home.
- F. Noninvasive devices to assess exposure to chemical and viral agents for children and adults and transmit this information to health care personnel for assessment and evaluation.
- G. Technologies to disseminate research information (i.e., biobehavioral responses, communication of risk, bioethics) to nurses practicing in emergency settings and in the community.

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### NATIONAL CENTER FOR RESEARCH RESOURCES (NCRR)

NCRR supports primary research to create and develop critical resources, models, and technologies. NCRR funding also provides biomedical researchers with access to diverse instrumentation, technologies, basic and clinical research facilities, animal models, genetic stocks, biomaterials, and more. These resources enable scientific advances in biomedicine that lead to lifesaving drugs, devices, and therapies.

For additional information about areas of interest to NCRR, please visit our home page at <http://www.ncrr.nih.gov>.

### Research and Development in Instrumentation and Specialized Technologies for Biomedical Research

- A. New or improved instruments, devices, and related methodologies to facilitate biomedical or behavioral research. Instrumentation includes but is not limited to mass spectrometry, nuclear magnetic resonance, electron spin resonance, fluorescent or kinetic or laser spectroscopies, X-ray absorption/ diffraction, electron or confocal or atomic force microscopies, and flow cytometry.
- B. Development of computer science/technology to study biomedical or behavioral research problems, e.g., computer visualization (graphics and virtual reality environments), image processing, computer modeling/ simulation including neural networks, structure-based drug design; development of new bioinformatics technology infrastructure.
- C. Biomedical engineering approaches for basic/clinical research that have potential for preventing or treating disease and/or significantly reducing health care costs, e.g., biomaterials, microsensors, monitoring devices, non-invasive diagnostic approaches, alternatives to radioactive-based methods, robotics, and drug delivery systems.

Electron Microscopy, X-ray Diffraction, Other Topics

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Imaging, EPR

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NMR, Optical Microscopy, Laser Applications

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Mass Spectrometry

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Computation, Bioinformatics

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### Research and Development in Comparative Medicine

- A. Development of improved reagents and cost-effective methods to accurately screen and diagnose selected laboratory animal diseases, and for performing overall assessments of animal quality and health status. An urgent need currently exists for the development of improved methods for the detection of active tuberculosis in nonhuman primates.
- B. Development of improved reagents and techniques for isolating and propagating embryonic stem cells (ESC), as well as fetal and adult stem cells from laboratory animals. Improved methods for causing ESC and other types of animal stem cells to differentiate along specific pathways in vitro and in vivo.
- C. Development of improved reagents, techniques, and equipment for isolating, propagating and characterizing specific gene sequences cloned in bacterial artificial chromosome (BAC) vectors and for preparing and characterizing BAC libraries made from laboratory animals.

- D. Development of improved reagents, techniques and equipment for preparing and analyzing full-length cDNA libraries made from tissues or cells of laboratory animals.
- E. Development of new technologies to rapidly phenotype large number of mutant animals.
- F. Development of vaccines and new therapeutic agents for the prevention and/or control of selected laboratory animal diseases. One high priority need is for the development of methods to control and prevent Herpesvirus B in nonhuman primates.
- G. Development of commercially valuable reagents for lower organisms or established cell cultures.
- H. Development of cost-effective methods for culture and/or preservation of commercially valuable organisms, including specific types of bacteria and other microorganisms.
- I. Development of cost-effective husbandry and colony management techniques, equipment, and/or new approaches to improve laboratory animal welfare and assure efficient and appropriate research use.
- J. Design of specialized equipment and caging for laboratory animals to permit optimal environmental control.
- K. Identification, development, and characterization of spontaneous and engineered vertebrate animal models for studies on various types of human disease. A need exists for a small animal model of Hepatitis C virus infection in humans.
- L. Development and refinement of new technologies for the effective cryopreservation and long-term maintenance of laboratory animal embryos, gametes, and their predecessors.
- M. Development of improved reproductive biology techniques (e.g., cloning techniques; embryo splitting) to produce genetically identical laboratory animals.
- N. Development of technologies for improved embryo transfer within a single animal species or of intraspecific embryo transfer to allow preservation of rare, unique, or endangered animal species that may have unique value as animal models for human disease.
- O. Development of improved reagents, techniques, and equipment for performing and

analyzing the results of microarray experiments.

Dr. Franziska B. Grieder  
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### Clinical Technology Applications

- A. Development of patient-oriented research technologies. This includes therapies, diagnostics, sensors, and imaging technologies used for patient diagnosis, monitoring, and treatment.
- B. Diversification of methods used for clinical studies of disease states, such as micro-analytical sensors or imaging devices.
- C. Miniaturization of existing biomedical technologies for adaptation to pediatric use.
- D. Development of artificial tissues and organs for medical use. Development of transplant technologies and human cell isolation techniques.
- E. Development of vehicles for drug delivery, including for patient groups with a potential for altered pharmacology or compliance, such as children or the elderly.
- F. Development of bioinformatics technology: (1) collection, collation, and archiving of databases; (2) assuring compatibility with other databases; (3) protected storage and transmission of confidential medical data; and (4) software which facilitates the review or implementation of clinical trial protocols; (5) software and hardware applicable to tying in data from multiple and simultaneous clinical protocols across multiple clinical sites; and (6) methods and instrumentation to support clinical imaging data.
- G. Development of vectors for gene therapy, with improved means of: (1) targeting specific cells and/or tissues; (2) transduction and expression; (3) delivery to patients; and/or (4) production and purification.
- H. Development of DNA microarray chip technology for studies of human diseases and methods and techniques for the analyses, storage, and interpretation of accumulated data.

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### Development of Discovery-Oriented Software and Tools for Science Education

Development of new discovery-oriented educational software and the application of educational technology and tools for education on health science topics that targets K through 12 students and undergraduate students are sought. Topics can range from basic molecular and cellular biology to human diseases. Development of this software may be directed toward the adaptation of existing or recently developed educational programs for interactive learning. This effort is intended to yield efficient and user-friendly educational units for K-12 and undergraduate students that can be extended to enhance the health science literacy of the general public. A broad dissemination is strongly encouraged.

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### Other Research Topic(s) Within the Mission of the Center

For additional information on research topics, contact:

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### NATIONAL CENTER FOR COMPLEMENTARY AND ALTERNATIVE MEDICINE (NCCAM)

The mission of the National Center for Complementary and Alternative Medicine (NCCAM) is to explore complementary and alternative healing practices in the context of rigorous science; educate and train complementary and alternative medicine (CAM) researchers; and disseminate authoritative



information to the public and professionals. CAM encompasses those healthcare and medical practices that are not currently an integral part of conventional medicine. The list of practices that are considered CAM changes continually as CAM practices and therapies that are proven safe and effective become accepted as "mainstream" healthcare practices. NCCAM groups these practices within five major domains: (1) alternative medical systems (for example, Traditional Chinese Medicine, Ayurveda); (2) mind-body interventions, (for example, meditation, biofeedback); (3) biologically-based treatments (for example, herbal therapies, special diets); (4) manipulative and body-based methods (for example, chiropractic, massage); and (5) energy therapies (for example, Reiki, Qi gong). For examples of each CAM domain in addition to the few provided above, see <http://nccam.nih.gov/about/plans/fiveyear/index.htm>, (pp. 25-27.)

The following narrative indicates the scope of projects suitable for SBIR/STTR projects that fit within the mission of NCCAM. For additional information about areas of interest to NCCAM and a listing of NCCAM's currently funded applications, please visit <http://nccam.nih.gov>.

### **Technology Development and Research**

NCCAM encourages innovative basic, pre-clinical, and early phase clinical studies that can ultimately lead to a commercializable CAM product. Included are applications that propose to develop and validate methods for chemical and biological identification of active ingredients in natural products, their mechanisms of action and interaction, bioavailability, and distribution, and to develop standardized, research-grade natural products.

### **Other Research Topic(s) Within the Mission of the Center**

For additional information on research topics, contact:

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### **NATIONAL CENTER ON MINORITY HEALTH AND HEALTH DISPARITIES (NCMHD)**

"The general purpose of the National Center on Minority Health and Health Disparities (NCMHD) is the conduct and support of research, training, dissemination of information, and other programs with respect to minority health conditions and other populations with health disparities" (P.L. 106-525). Within the NIH, the NCMHD serves as the focal point for planning and coordinating minority health and other health disparities research. The Center coordinates the development of a comprehensive health disparity research agenda that identifies and establishes priorities, budgets, and policy that govern the conduct and support of all NIH sponsored minority health and other health disparities research and training activities.

For additional information about the areas of interest to the NCMHD, please visit our home page at <http://www.ncmhd.nih.gov>.

### **Broad Area of Research that we Support**

Studies on the biological and biobehavioral risk factors for disparities in health and health outcomes; cultural, environmental, and societal dimensions of disparities in health status, including the impact of health processes; development and refinement of research tools, survey instruments, and databases that are culturally sensitive and specifically for racial and ethnic minority populations and other health disparity populations, in particular the medically underserved which includes the rural and urban poor.

For additional information on research topics, contact:

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### **NATIONAL LIBRARY OF MEDICINE (NLM)**

The NLM supports research and development projects in biomedical informatics as applied to clinical, research, educational, or administrative areas of health care.

For additional information about areas of interest to the NLM, please visit our home page at <http://www.nlm.nih.gov/ep/extramural.html>.

#### **Bioinformatics**

The appearance of new scientific research methods has greatly increased the volume of molecular data for all the basic medical sciences. To help manage such data, NLM is interested in:

- A. Software algorithms and database query methods capable of translating natural language questions into appropriate retrievals from multiple related factual databases.
- B. Software for data management and analysis for genetic linkage mapping, physical mapping, DNA sequencing, and proteomics.
- C. Expert system techniques for automatic generation of annotation information and creation of linkages among related databases via explicit pointers or common vocabulary.
- D. Algorithms capable of predicting structure and/or function in model biological systems.

#### **Medical Informatics**

There are broad needs for innovative computer software and systems to assist changing dimensions of health care by developing knowledge bases,

information synthesizing mechanisms, decision support systems, and similar modalities. NLM is interested in:

- A. Mechanisms to integrate new information into existing knowledge bases, and software to extract and analyze information from large patient record databases (i.e., secondary data aggregation).
- B. Development of organizing and synthesizing systems that closely match specific health problem areas to help health care providers manage information better.
- C. Systems, devices, or programs that facilitate utilization of electronic medical record systems in clinical practice, for such functions as chart entry, ordering, and scheduling.

Projects relevant to the informatics of disaster management or to reduction of medical errors are particularly encouraged.

### **Other Research Topic(s) Within the Mission of NLM**

For additional information on research topics, contact:

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### **CENTERS FOR DISEASE CONTROL AND PREVENTION (CDC)**

**CDC will accept SBIR grant applications ONLY on the April 1, 2003 and December 1, 2003 receipt dates.**

The CDC serves as the national focus for developing and applying disease prevention and control, environmental health and health promotion and health education activities designed to improve the health of the people of the United States. To

accomplish its mission, CDC identifies and defines preventable health problems and maintains active surveillance of diseases through epidemiologic and laboratory investigations and data collection, analysis, and distribution; serves as the PHS lead agency in developing and implementing operational research aimed at developing and testing effective disease prevention, control and health promotion programs; administers a national program to develop recommended occupational safety and health standards and to conduct research, training, and technical assistance to assure safe and healthful working conditions for every working person; develops and implements a program to sustain a strong national workforce in disease prevention and control; conducts a national program for improving the performance of clinical laboratories; and develops programs to prevent premature death and avoidable illness and disability caused by noninfectious, non-occupational environmental and related factors.

CDC is responsible for controlling the induction and spread of infectious diseases, and provides consultation and assistance to other nations and international agencies to assist in improving their disease prevention and control, environmental health, and health promotion activities.

For additional information about areas of interest to the CDC, please visit our home page at <http://www.cdc.gov>.

### **NATIONAL INSTITUTE FOR OCCUPATIONAL SAFETY AND HEALTH (NIOSH)**

The NIOSH plans, directs and coordinates the national program effort to develop and establish recommended occupational safety and health standards and to conduct research, training, and related activities to assure safe and healthful working conditions for every working man and woman. NIOSH has both a regular grant program and an SBIR grant program; the purpose of both is to develop knowledge that can be used in preventing occupational diseases and injuries. In the regular NIOSH grant program, the following types of applied research projects are supported: causal research to identify and investigate the relationships between hazardous working conditions and associated occupational diseases and injuries; methods research to develop more sensitive means of evaluating hazards at work sites, as well as methods for measuring early markers of adverse health effects and injuries; control research to develop new

protective equipment, engineering control technology, and work practices to reduce the risks of occupational hazards; and demonstrations to evaluate the technical feasibility or application of a new or improved occupational safety and health procedure, method, technique, or system.

### **Control Technology and Personal Protective Equipment**

Engineering controls, administrative policies, and personal protective equipment are needed to manage exposures to occupational hazards. Engineering controls include substitution of a safe material for a hazardous one, design changes to equipment, or modification of work methods to eliminate or reduce hazards. Changes in work practices and management policies and training programs are examples of administrative controls. In some cases where it is not otherwise possible to maintain a healthy work environment, personal protective equipment such as respirators and protective clothing can be used to isolate workers from the hazard. Research is needed to develop and evaluate control strategies for specific hazards and to assure their practicality and usability in workplaces.

- A. Investigate the effectiveness of existing or proposed engineering controls (including retrofit solutions).
- B. Develop control measures for new workplace hazards.
- C. Identify the specific hazardous parts of a job that contribute most to the actual exposure, including personal hygiene where contamination of surfaces, clothing, or skin may occur.
- D. Evaluate the practical utility in the workplace of proposed personal protective equipment, when it is the only available control option.
- E. Design personal protective equipment that will fit the anthropometric diversity in today's workforce.
- F. Develop alternatives to pesticide application and hazardous waste remediation.
- G. Develop micro sensing devices to notify workers before chemicals break through protective clothing and identify failures in containment systems for hazardous materials.
- H. Create and test new materials for clothing to protect against chemical and physical hazards.

- I. Develop information dissemination methods to help businesses learn about and implement occupational safety and health programs.
- J. Design and evaluate training materials to teach hazards and risks, demonstrate solutions, measure changes in behavior and practices, and improve injury and illness rates.

### Exposure Assessment Methods

Exposure assessment is a multi-disciplinary field central to deciding whether and how to use resources for reducing workplace exposures, and to defining exposure-response relationships in epidemiologic studies. Rapid, inexpensive measurement tools and improved data analysis methods are needed for the collection of adequate exposure data and for effective intervention. At least three major gaps in current methods will drive development of exposure assessment methods in the next decade: (1) the lack of sufficiently precise exposure assessments to support accurate epidemiologic studies in the complex environments of today's workplaces, (2) the lack of practical measurement techniques that can be applied at reasonable cost in many workplaces where hazards may exist, and (3) the lack of validated methods for measuring relevant exposure and total dose data directly from biological samples obtained by relatively noninvasive techniques.

- A. Develop computer models to extrapolate information from historical data of limited exposure measurements to apply to large study populations, and to incorporate short-duration but high-intensity exposures such as leaks or spills into the models.
- B. Develop easy-to-use, direct-reading instruments and test kits to measure exposures rapidly and inexpensively in a variety of workplaces for routine monitoring, evaluating the success of control technologies, and providing data for research studies.
- C. Improve the measurement of low concentrations of chemicals and biomarkers in biological specimens such as blood, urine, saliva and sweat so that such concentrations can be linked to internal dose at the target organs.
- D. Design laboratory analytical methods for inexpensively measuring numerous chemicals in a single sample.

- E. Improve the measurement and interpretation of biomarkers to facilitate evaluation of the effects of structurally similar chemicals.
- F. Formulate exposure survey designs and methods for exposure data analysis to obtain more meaningful data for health risk assessments.
- G. Improve exposure assessment methods so that at-risk workers can be identified, the most cost-effective control and intervention strategies can be determined, better understanding can be gained about exposure-response relationships, and improved baseline data can be collected for standard setting and risk assessment.

### Intervention Effectiveness Research

The goal of intervention research is to develop practical strategies and techniques that effectively reduce or prevent workplace injuries and illnesses. Workplace safety and health interventions include but are not limited to developing and implementing specific engineering control technologies, process and work organization changes, information dissemination and health communication practices, worker/management participatory safety and health programs, safety and health training, selective use of personal protective equipment, and inspection and enforcement of protective exposure limits. Intervention research involves the testing and evaluation of interventions, programs, and policies. Although many intervention strategies have been applied to industrial settings, knowledge about what works best is limited. Corporate safety and health programs, regulatory requirements and voluntary consensus standards, workers' compensation policies and loss-control programs, engineering controls, and educational campaigns are among the types of interventions that need to be developed, implemented, and evaluated.

- A. Develop techniques to evaluate the effectiveness of implemented control technologies.
- B. Determine the barriers to the acceptance of new control technologies and develop approaches to eliminate or alter these barriers, including economic feasibility.
- C. Determine the factors that influence the voluntary adoption of protective work practices.
- D. Evaluate the roles of researchers, consultants, trainers, worker organizations, and industry trade groups as partners in intervention efforts.

- E. Investigate organizational and economic factors that could predict success in prevention programs, and how these programs can be tailored to take account of such factors.
- F. Develop strategies for targeting intervention efforts in the areas of greatest need.
- G. Investigate why managers and workers in some organizations implement occupational safety and health programs when others do not.

### Surveillance Research Methods

Surveillance systems describe where occupational hazards, injuries, or illnesses are found, how frequently they are found, whether they are increasing or decreasing, and whether prevention efforts have been effective. The public health community relies on surveillance information to set research and prevention priorities, but critical gaps in current systems limit their usefulness. These systems need to be updated and expanded, and new systems and methodologies need to be developed.

- A. Develop approaches for implementing comprehensive, integrated national systems utilizing data sources and models of surveillance that exist in the public and private sectors.
- B. Formulate methods to assess nationally or locally the impact of intervention efforts on worker safety and health.
- C. As restructuring of health care delivery systems occurs throughout the United States, develop linkages among the systems to identify, track, and target occupational safety and health problems and provide information for decisions to develop interventions or to improve related medical care.
- D. Investigate hazard surveillance systems as a means of identifying risks and exposures at worksites and industries, including risks associated with prototypes of new technologies, before injuries and illnesses occur.

### Other Research Topic(s) Within the Mission of the Institute

For technical information on research topics, contact:

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For administrative and business management information, contact:

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### NATIONAL CENTER ON BIRTH DEFECTS AND DEVELOPMENTAL DISABILITIES (NCBDDD)

The National Center on Birth Defects and Developmental Disabilities at the Centers for Disease Control and Prevention seeks to promote optimal fetal, infant, and child development; prevent birth defects and childhood developmental disabilities; and enhance the quality of life and prevent secondary conditions among children, adolescents, and adults who are living with a disability.

The NCBDDD areas of interest focus on:

- A. Develop, produce and evaluate the effectiveness of an educational video/CD-Rom/instructional module about the importance of pre-concept ional folic acid. Target audiences include but are not limited to: engaged couples; high school and college students, beauty spa and salon employees, health professionals such as nurses and

nutritionists, newly married couples, Hispanic women, and all women of reproductive age.

- B. Design, test and produce a symbol or graphic that communicates clearly and effectively that a medication has teratogenic properties. The symbol should be tested within a variety of audiences, and not subject to harmful misinterpretation. Phase 2: develop and test the effectiveness of a health communication module (in any format) to explain the concept of teratogenicity and educate young women of childbearing age about the dangers of sharing medications
- C. Develop a meal replacement formula appropriate for patients with PKU that improves upon current acceptability related to taste, convenience and cost.
- D. Conduct a feasibility study regarding the development of time-release formula folic acid supplements so that they could be taken less frequently than once per day (e.g., once per week, or every few days) and still meet the U.S. PHS recommendation for women of 400 mcg daily on an average basis.
- E. Develop and format a folic acid physician's clinical counseling module for personal data assistants (PDAs). Develop and evaluate a dissemination plan for encouraging physicians' use of PDAs as an educational tool for folic acid and other preconceptional health messages.
- F. Conduct risk analysis research to determine the potential effects of recently increased prescription of valproic acid (a teratogen) for bipolar disorder, often diagnosed in child bearing age women. Analysis should include risks and benefits of alternative therapies.

#### **Other Research Topic(s) Within the Mission of the Center**

For additional information on research topics, contact:

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#### **NATIONAL CENTER FOR CHRONIC DISEASE PREVENTION AND HEALTH PROMOTION (NCCDPHP)**

The NCCDPHP plans, directs, and coordinates programs in health promotion, chronic disease prevention, and reproductive health to enhance quality of life, improve reproductive health, and reduce the incidence of heart disease, stroke, cancer, diabetes, arthritis, obesity, oral disease, infant and maternal morbidity and mortality, unintended pregnancy, and emerging chronic diseases. NCCDPHP uses two essential criteria to prioritize its research portfolio, societal burden and disproportionate burden. NCCDPHP places high priority on chronic diseases and conditions and reproductive health outcomes that have the greatest total impact on health, longevity, and quality of life. NCCDPHP places high priority on eliminating disproportionate burden related to sex, age, race, ethnicity, geography, sexual orientation, socioeconomic status, disability, and special needs. NCCDPHP supports three primary types of applied research, research on cause (determinant research), research on effect (intervention research), and research on application and benefit (dissemination research). NCCDPHP emphasizes cross-cutting research that is participatory, accounts for social and ecological factors, and is implemented at multiple levels.

NCCDPHP has identified ten priority research areas: (1) develop new measures and research designs to strengthen the quality of research; (2) identify the underlying determinants of racial and ethnic health disparities; (3) develop and evaluate interventions to eliminate health disparities; (4) examine established and emerging risk factors for chronic disease and investigate their potential for public health interventions; (5) assess the effectiveness of policy and environmental interventions to promote health; (6) improve the processes and outcomes of health care systems; (7) develop effective communication strategies to promote health; (8) examine methods for helping people manage their own health; (9) develop and evaluate the effectiveness of population-based health promotion and disease prevention policies and programs at the local, state, national, and international levels; (10) examine approaches for effectively translating successful community interventions into widespread practice. For examples of specific research questions in each



of the ten priority areas, see *Setting the Agenda: CDC Research in Chronic Disease Prevention and Health Promotion*, available at <http://www.cdc.gov/nccdphp/agenda/index.htm>.

For technical information on research topics, contact:

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### Office on Smoking and Health

The Office on Smoking and Health, National Center for Chronic Disease Prevention and Health Promotion, in collaboration with the National Center for Environmental Health (NCEH) are working to collect, analyze, and disseminate data relating to the effect of cigarette smoking on human health and to develop methods for improved information related to smoking and health. Part of this effort involves the laboratory analysis of cigarettes by the Air Toxicants Branch, NCEH.

Understanding the design and construction of cigarettes is integral to research into the health consequences of smoking. Changes in product composition or design (e.g., the presence or absence of an additive, tobacco cut-width, smoke pH, degree of ventilation) can influence the toxicity of cigarette smoke. Consequently it is necessary to separate cigarette components (e.g., reconstituted sheet) in order to determine their chemical composition and evaluate their contribution to levels of nicotine and other toxic chemicals in smoke. Separating the cigarette filler components by hand with magnification is difficult and time-consuming, hampering efforts to obtain sufficient material for research purposes.

Applications are invited for the development of a method (i.e., method, technique, instrument, or device) to separate cigarette filler consisting of tobacco and tobacco-derived components (i.e., bright, burley, and Oriental tobacco, stems, puffed tobacco, paper reconstituted tobacco, and bandcast reconstituted tobacco). The method should also be applicable to other combustible tobacco products such as bidis, clove cigarettes, and cigars. The method should be of sufficiently high through-put to

allow practical quantities of tobacco and tobacco-derived components to be separated in less than 24 hours. An example of a practical quantity is the amount of tobacco and tobacco-derived materials contained in a pack (i.e., 20 cigarettes) of cigarettes. Each separated fraction should contain less than 5% carry-over of other materials.

The application should discuss (1) a plan to develop a method (i.e., method, technique, instrument, or device) to separate the various tobacco and tobacco-derived components of the combustible cigarette column (i.e., bright, burley, and Oriental tobacco, stems, puffed tobacco, paper reconstituted tobacco, and bandcast reconstituted tobacco); (2) documentation of the capacity and the accuracy of the method; (3) verification of the identity of the separated fractions and the degree of carry-over by light microscopy; and, (4) evidence that the method, device, or technique is applicable to all current varieties of American-style blended cigarettes and potentially applicable to other combustible tobacco products such as bidis, clove cigarettes, and cigars. The invited applications will not involve human subjects.

### Epidemiology Branch

**Method to screen tobacco products for reduced-harm or reduced-exposure claims.** Applications are invited for the development of the technology that will lead to a method or methods to rapidly, yet accurately, monitor claims of lowered levels of specific chemicals in tobacco products (i.e., "reduced-exposure" or "reduced-emission" products) and evaluate made or implied reduced-harm claims (e.g., respiratory tract toxicity and cancer).

Cigarette smoking is a cause of coronary heart disease, atherosclerotic peripheral vascular disease, cerebrovascular disease, cancers of the lung, larynx, mouth, esophagus, and bladder, chronic obstructive pulmonary disease, intrauterine growth retardation, and low-birth weight babies. The Centers for Disease Control and Prevention (CDC) is engaged in activities to collect, analyze, and disseminate data relating to the effect of cigarette smoking on human health and to develop methods for improved information related to smoking and health.

Since the late 1980's, cigarette manufacturers have begun to market and sell "reduced-exposure" products. For example, the tobacco industry regularly advertises that some products present less risk of certain smoking related diseases. These



advertisements purport that the best alternative to quitting is using a "less risk" product.

Introduction of products that promise reduced exposure and reduced harm may increase initiation and increase, decrease, or have no effect on quit attempts. It is also conceivable that these products may increase relapses among former smokers that would smoke again if the health risks of cigarettes were perceived as being eliminated. To design successful public health programs that address new and emerging tobacco product technologies, information is needed on how these products compare to traditional cigarettes with respect to toxicity and smoke chemistry. Stated claims of lower yields of specific chemicals need to be verified under conditions relevant to how the product is smoked by people, this in addition to the Federal Trade Commission method which uses an automated smoking machine. Technologies such as those used in a self-extinguishing cigarette need to be monitored for an overall increase in the harmfulness of the product. A research tool is needed that allows researchers to quickly evaluate and react to tobacco product claims and new technologies.

Applications are invited for the development of the technology that will lead to a method (i.e., method, technique, instrument, or device) or methods to rapidly, yet accurately, monitor reduced-harm and reduced-exposure tobacco product claims. The method should address claims of lowered levels of specific chemicals in the smoke (e.g., nicotine or tobacco-specific nitrosamines) of tobacco products. The method should also employ technology to evaluate made or implied reduced-harm claims (e.g., respiratory tract toxicity and cancer). The method should be applicable to a wide variety of tobacco products including self-extinguishing cigarettes, and modified emission (i.e., "reduced-exposure") products. The method must allow comparisons with traditional cigarettes or experimental reference cigarettes (e.g., Kentucky reference cigarettes). When fully developed, the method should be of sufficiently high through-put to allow a practical number of brands to be investigated and results to be generated in a reasonable length of time. At least 5 brands is considered a practical number of brands. A reasonable length of time is considered 3 to 6 months to conduct the tests. The invited applications will not involve human subjects.

## Other Research Topic(s) Within the Mission of the Institute

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## Division of Adult and Community Health

The mission of the Division of Adult and Community Health, NCCDPHP, has seven major components:

1. **Aging.** CDC has established national, state-based programs targeting cardiovascular disease, diabetes, cancer, arthritis, injuries, and immunization. CDC's unique expertise can be readily applied to target the health needs of older Americans by providing public health leadership and coordination, by enhancing surveillance, and by putting research to work for older Americans.
2. **Arthritis.** Arthritis and other rheumatic conditions currently affect nearly 43 million

Americans, or about one of every six people. As the nation's population ages, arthritis is expected to affect 60 million people by 2020. The leading cause of disability in the United States, arthritis is estimated to cost almost \$65 billion annually in medical care and lost productivity. Although prevailing myths have portrayed arthritis as an inevitable part of aging that can only be endured, effective interventions are available to prevent or reduce arthritis-related pain and disability.

3. **BRFSS.** Behavioral Risk Factor Surveillance System, The BRFSS, the world's largest telephone survey, tracks health risks in the United States. Information from the survey is used to improve the health of the American people.
4. **Cardiovascular Health.** Killing almost a million Americans each year, cardiovascular disease - principally high blood pressure, heart disease, and stroke - is the leading cause of death among both men and women, and across all racial and ethnic groups. About 58 million Americans live with some form of the disease. In 1999 alone, cardiovascular disease cost the nation an estimated \$287 billion in health care expenditures and lost productivity, and this burden is growing as the population ages. A limited number of health-related behaviors - most notably tobacco use, lack of physical activity, and poor nutrition - are responsible for much of the burden of cardiovascular disease.
5. **Epilepsy.** Epilepsy is a chronic neurological condition affecting about 2.3 million Americans. Approximately 181,000 people are diagnosed with epilepsy and seizures each year. For the vast majority of epilepsy cases, no single cause has been determined.
6. **Health-Related Quality of Life Surveillance.** In public health and medicine, the concept of health-related quality of life refers to a person's or group's perceived physical and mental health over time. Tracking health-related quality of life in different populations can identify subgroups with poor physical or mental health and can help guide policies or interventions to improve their health.
7. **Prevention Research Centers.** Prevention Research Centers strive to improve health promotion and disease prevention efforts by focusing on high-priority public health issues, bridging gaps between scientific knowledge

and public health practice, applying and rapidly transferring research results, and enhancing cooperation between academic institutions and state and local health departments.

Areas of interest include but are not limited to:

- A. **Epilepsy and Seizures.** Epilepsy and seizures affect approximately 2.3 million Americans of all ages. It is estimated that approximately 10% of the American population will experience a seizure in their lifetimes; 3% will develop epilepsy by age 75. The Epilepsy Program in the Division of Adult and Community Health is working to implement program activities related to the epilepsy consensus priorities developed at the first national conference on public health and epilepsy in 1997. These priorities have formed the basis for CDC epilepsy program activities in the areas of improving care, improving communication and combating stigma, self management, disease surveillance and prevention research, increasing public awareness and knowledge, and strengthening partnerships.
- B. **Physician and Other Health care Provider Education/Training**
  1. Methods are needed to increase awareness of the importance of epilepsy self management. Programs are needed to build self management education, including the promotion of self efficacy and adoption of healthy personal behaviors, into routine care for people with epilepsy and seizures.
  2. Design, develop and evaluate materials to educate or train physicians and/or other health care professionals on the importance of enhancing the self efficacy and empowerment of persons with epilepsy and seizures, and on how to foster increased self management among their epilepsy patients.

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### Division of Diabetes Translation

The Division of Diabetes Translation (DDT) supports applied research on assessing the burden of diabetes, the prevention and early detection of diabetes, the treatment of its complications, improving the quality of and access to diabetes care, and developing and evaluating new approaches to improve care for persons with diabetes. CDC supports diabetes control programs in all 50 states, the District of Columbia, and 7 U.S. territories to increase awareness and education about diabetes, promote early detection of diabetes and treatment of its complications, and improve the quality of and access to diabetes care for all persons with diabetes. CDC and the National Institutes of Health jointly sponsor the National Diabetes Education Program. DDT's research portfolio targets several special populations, including children, women, American Indians, African Americans, Hispanics/Latinos, and Asian American/Pacific Islanders, and addresses the burden of diabetes along the U.S./Mexico border and internationally.

- A. **Development and Evaluation of Innovative Community Approaches for Self-Management Training.** As reviewed recently (see Norris et al., *Diabetes Care* 2001; 24:261-87), evidence supports the short-term effectiveness of self-management training in type 2 diabetes, but research is needed to assess the long-term effectiveness of such interventions on glycemic control, development of microvascular and macrovascular disease, and quality of life, especially for self-management training conducted in community settings, rather than clinics and other health-care settings. DDT solicits research applications to develop and evaluate (1) optimal methods of delivery of home-based interventions (including but not limited to the roles of family, lay health-care workers such as promotoras, and computer-assisted instruction); and (2) approaches for identifying persons who would benefit from community approaches, maximizing participation and retention, and linking interventions with primary

care. DDT encourages research to explore how settings, providers, and specific intervention characteristics (content, duration, frequency) interact to achieve optimal results in diverse populations and settings. Research is also needed to compare barriers and effectiveness of interventions in community settings and clinics, especially for high-risk minority populations. Research to examine the relative costs and prevention effectiveness of different approaches and potential mechanisms for integration within health-care systems will also be considered.

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- B. **Role of Lipoprotein Subfractions in Risk for Complications of Diabetes.** As summarized by the American Heart Association, diabetes is a major independent risk factor for cardiovascular complications, including coronary heart disease, stroke, peripheral artery disease, nephropathy, retinopathy, and possibly neuropathy and cardiomyopathy (see Grundy et al., *Circulation* 1999;100:1134-46). Diabetes causes preventable complications that can be life-threatening, including kidney disease and amputations; the most serious complications are associated with macrovascular and microvascular disease. In addition, cardiovascular disease is the major cause of mortality in persons with diabetes, including women. Recent research findings indicate that ischemic heart disease risk varies, even among normocholesterolemic persons, according to concentrations of various LDL, HDL, and VLDL subfractions. However, because measurement of lipoprotein subfractions is time-consuming, labor intensive, and requires sophisticated instrumentation, these determinations are not widely performed, and few data are available for persons with diabetes. In addition, different research laboratories use different analytical approaches and no reference method or standard reference material is available, so results vary among laboratories and may not be comparable.

Newer analytical methods, including NMR, have shown promise in addressing these limitations.

DDT solicits applications for research to (1) describe lipoprotein subfraction distributions and their associations with other cardiovascular risk factors in persons with diabetes, (2) evaluate the role of lipoprotein subclasses and particle size as risk factors for the development of macrovascular and microvascular complications in persons with diabetes, and (3) determine the impact of improved diabetes care (including better glycemic control, use of hypoglycemic and other medications, and lifestyle interventions) on lipoprotein subclasses. Because of the recent emergence of type 2 diabetes in children and adolescents, especially in minority populations, research applications to explore lipoprotein subclasses in children and adolescents with diabetes are encouraged. Applications for research to examine lipoprotein subfraction distributions and their correlates in persons at increased metabolic risk for diabetes, including individuals with insulin resistance, impaired fasting glucose, and impaired glucose tolerance, will also be considered.

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C. **Methodology for Imputing Missing Data in Nationally Representative Surveys.**

Statistical methods to analyze datasets that have missing data have been available for several years (see Schafer, 1977). These methods are rarely used in public health and epidemiologic research, although missing data are ubiquitous. Research on developing, implementing, and testing new methods for imputing missing data has the potential to improve survey research and to improve public health practice and policy making, which is often based on survey data. DDT is specifically interested in encouraging methods research for imputing income data and race/ethnicity data, which are often missing in large population-based surveys such as the Behavioral Risk

Factor Surveillance System (BRFSS) and the National Inpatient Sample (NIS), respectively.

Schafer JL. *Analysis of Incomplete Multivariate Data*. London: Chapman & Hall, 1977.

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D. **Validation of Measuring Diabetes Preventive Care Practices.**

Diabetes-related preventive care practices (e.g., self-care and physician practices such as annual foot and eye exams, hemoglobin A1c testing, and diabetes self-management education) have the potential to prevent or delay the development of complications from diabetes. Because of the critical importance of preventive care practices, diabetes surveillance systems and initiatives to improve quality of diabetes-related care monitor trends in preventive care practices. The validity (e.g., sensitivity, specificity, predictive value positive) and reliability of methods using interview data, administrative data, and medical records to measure the delivery or receipt of preventive care practices have not been well characterized. However, some studies have suggested that the specificity of preventive care practices is not high, their sensitivity depends on the measure or indicator, and that medical record review is an imperfect gold standard for assessing validity. A greater understanding is needed of the validity and reliability issues surrounding the measurement of preventive care practices for persons with diabetes. DDT encourages research to characterize and summarize these measurement issues and to develop, compare, and evaluate new approaches to improve measurement of preventive care practices, including comparison of the sensitivity, specificity, predictive value positive, and reliability of general and diabetes-related preventive care practices.

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### Division of Oral Health

Providing Safe Dental Care Infection control in the dental care environment remains essential to ensuring the public's safety and retaining its confidence. In the 15 years since CDC published its first guidelines for infection control in dentistry, infection control practices have dramatically improved. Nevertheless, the potential for disease transmission during visits to the dentist continues to arouse intense public interest and media scrutiny. To minimize this potential, CDC assesses the risks of infectious disease transmission, updates guidelines to minimize those risks, investigates disease outbreaks and environmental hazards in the dental setting, and identifies emerging problems. Infection control activities address the "Healthy People 2010" priority areas in Occupational Safety and Health, Immunization and Infectious Diseases, and HIV Infection.

- A. There are approximately 600,000–800,000 needle stick and other sharps injuries each year among the twelve million health care workers in the United States. Each sharps injury carries the risk of exposure to infectious blood borne diseases, such as such as the Human Immunodeficiency Virus (HIV), Hepatitis B virus (HBV), or Hepatitis C virus (HCV). There is an effective immunization against HBV, but none for HIV or HCV. Prevention relies on elimination of needle stick and sharps injuries. The Needle stick Safety and Prevention Act, signed into law on November 6, 2000, requires health care facilities under the federal OSHA to use "safer medical devices, such as sharps with engineered sharps injury protections and needleless systems." These include blunt needles, or those that otherwise retract or shield the sharp point or edge after use.

The purpose of this research initiative is to develop a safety syringe to administer anesthesia during dental procedures that meets the desired clinical and performance criteria identified by CDC. The ultimate goal is to protect dental healthcare workers from needlestick and other sharps injuries thereby preventing unnecessary disease.

- B. Each year around the world, thousands of dedicated individuals and organizations—including the military, as well as governmental and private relief organizations—struggle to provide urgent and essential healthcare to underserved populations in a wide variety of non-traditional settings. On every continent, these caregivers are present in areas affected by poverty or devastated by war, ethnic conflict and natural catastrophe. Each of these scenarios presents unique challenges for the safe and effective delivery of healthcare. Significant among these challenges is control of the spread of infectious disease.

Efforts to prevent infections among patients and healthcare workers can be compromised by a host of factors including local disease prevalence (e.g., tuberculosis, HIV, HBV), lack of clean water, absence of modern facilities, equipment and supplies, as well as inadequate sanitation. Medical and dental teams operating under field conditions must balance the need for adequate infection control and healthcare worker protection against the urgent needs of the population they seek to assist. Stringent limitations on the size and weight of supplies and equipment—including sterilizers and liquid chemical germicides are often a fact of life for deployed medical personnel.

The purpose of this research initiative is to develop a chemical germicide that can be used under austere field conditions. This product should be a stable powder or concentrate that is mixed with water at the point of use to provide a high-level disinfectant/sterilant that is easy to use, environmentally safe and cost-effective.

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### Division of Cancer Prevention

The Cancer Surveillance Branch of the Division of Cancer Prevention and Control supports Cancer Registration activities in population based cancer registries. This national program with its partners encompasses the entire research, evaluation, collection, and analysis phases of cancer surveillance data for use in comprehensive cancer control plans.

- A. Promote the advancement and utilization of real-time standardized computerized interfacing

from Hospital Registry systems to medical record data sources and to Population based cancer surveillance systems. Activities would include improve the communication and computerized interface technology such as the establishment of Virtual Private Network, and secure Internet technologies to facilitate the secure reporting of data from providing organizations; innovations and application of mapping of local codes to national clinically relevant standard codes (such as LOINC and SNOMED) and vice-versa; advancement in the use of standardized reporting structures such as Health Level 7 (HL7) standards and Extensible Markup Language (XML).

- B. Develop innovative presentation of cancer research and surveillance data such as graphical information systems for the analysis of data, and improved innovation in the design and use of management reports.
- C. Promote the advancement and development of integrated person centered data repository with other appropriate data systems applying cancer registry data and other disease registries and vital records data.
- D. Develop innovative and automated computerized data quality improvements, such as the application of intelligent business rules for use in cancer registry applications. Such that when modification are adjusted to a patients cancer abstract all necessary modifications are done based on appropriate automatic quality control checks.
- E. Promote the development of probabilistic matching models for auto-encoding of narrative text based medical records sources such as narrative pathology, endoscopy, or surgery reports to standardized reporting codes.

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## **Division of Nutrition and Physical Activity**

The Division of Nutrition and Physical Activity is partnering with the National Cancer Institute (NCI), the Produce for Better Health Foundation (PBH), the United States Department of Agriculture (USDA), the American Cancer Society (ACS), and others on the 5 A Day for Better Health Program, an initiative to increase American's intake of fruit and vegetables. High intake of fruit and vegetables has been associated with reduced risk of cardiovascular disease, many cancers, as well as other chronic diseases and conditions. Further, over consumption of food combined with lack of physical activity is creating an epidemic of overweight and obesity in the United States. Opportunities exist to prevent or reduce the burden of many chronic diseases by increasing knowledge of nutrition, increasing availability of and access to healthy foods, and changing policies to promote healthful choices.

### **CHRONIC DISEASE NUTRITION**

There is interest in the development, dissemination, and evaluation of innovative methods to increase knowledge of healthful nutrition practices including increased fruit and vegetable intake, decreased fat intake, and decreased caloric consumption among persons of many different backgrounds and at different stages of life. Although effective strategies for nutrition education exist, few have been disseminated to a larger audience than the original research population. The focus of proposed projects should reflect target populations at high risk of developing nutrition related chronic diseases. There is also interest in the development of nutrition intervention programs that are targeted toward changing the environment or policies that affect people's food choices. Most nutrition interventions provide nutrition education for individual dietary change but do not change the environment or policies that affect a population's access to healthful foods. Some limited research has examined how the availability of and access to fruit and vegetables impacts consumption. Environmental and policy interventions to increase availability and reduce prices of fruit and vegetables have been effective in the short-term. Few of the interventions have lasted long enough to determine whether increased consumption could be sustained over the long-term.

- A. Use of innovative or new strategies to promote health.
  - 1. Design, develop, and evaluate a fruit and vegetable logo program that aids



consumers in determining servings of fruit and vegetables consumed. This program should complement the American Heart Association Healthy Heart program, where it exists. The Healthy Heart program has been successfully implemented in restaurants in Southwestern and Western states. This program could include a menu logo listing the servings of fruit and vegetables in certain healthful menu items, table tents promoting menu items that also include nutrition information, or coloring sheets and crayons with nutrition messages targeted to children. This program could be promoted for use in national chain restaurants as well as smaller, individual restaurants.

2. Design, develop, and evaluate methods to encourage purchase of simple, time saving, fresh, and good tasting healthful food items in supermarkets, convenience stores, or other locations. Some examples of supermarket methods include dinner of the day (i.e., a rack that conveniently contains all items needed for a healthy meal including recipe information), convenience meals, or healthy children's lunch packs. Some examples of convenience store methods include a rack at the front counter containing individually wrapped snack packs or items packaged to be eaten on the road (e.g., a fruit cup with spoon that can fit in an automobile drink holder).
3. Design, develop, and evaluate innovative food service alternatives for use at schools, workplaces, or other locations. Some examples include smoothie bars, salad bars, burrito bars, vending machine alternatives, or other similar options. Several of these food service alternatives have been tried in school systems across the country. This program would incorporate the practices that have been successfully implemented. Examples to follow include the Santa Monica Farmer's Market Salad Bar Program, innovative changes in food service in the Los Angeles County School System, and successful research interventions that changed availability and pricing in school or workplace cafeterias and vending machines.
4. Design, develop, and evaluate (pilot test) a comprehensive educational strategy/program with school aged children and young adults (preschool to college) that focuses on increased vegetable and fruit consumption. This comprehensive educational strategy/program may be school or community based. It should be interdisciplinary, have a multi-dimensional approach, be theory based and generalizable to the national population. Partnering is encouraged with those entities interested in improving community health. Examples of existing interventions include the Gimme 5, High 5 school-based interventions, and the Boy Scout 5 A Day badge project. Innovations may include interventions in other youth organizations or programs.
5. Environmental change interventions can be an effective way to support a community effort to increase community vegetable and fruit intake. Design, implement, and evaluate an environmental change intervention incorporating 5 A Day. This intervention should be an educational and ecological effort emphasizing such factors as access to vegetables and fruits, cost/pricing of vegetables and fruits, and point-of-purchase education. Behavior-specific ecological models should be used to guide this intervention. This intervention may use innovative methodology and partnering to facilitate consumption of vegetables and fruits and encourage physical activity near large public land-use areas (examples include: strategies for edible trails, landscapes and community gardens).

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#### **Division of Cancer Prevention and Control**

The National Center for Chronic Disease Prevention and Health Promotion supports a national program to prevent premature death and disability from chronic diseases and to promote healthy personal behaviors. Within the Center, the Division of Cancer

Prevention and Control supports comprehensive cancer surveillance, epidemiologic, health and behavioral science research, communications and program services to reduce the illness and death associated with cancer. The following are two ideas we suggest be incorporated into the Small Business Innovation Research call for proposals.

### **BREAST CANCER EARLY DETECTION**

The Breast and Cervical Cancer Early Detection Program in the Division of Cancer Prevention and Control is a national program to coordinate and improve the delivery of comprehensive breast and cervical cancer screening and diagnostic services to low income women who lack the income or insurance coverage necessary to participate in these potentially lifesaving procedures, with an emphasis on reaching women from minority populations who are less likely to have access to or participate in them. Breast cancer screening is directed to women age 40 and older. Women diagnosed with breast cancer are most likely to survive when their disease is detected at a very early stage.

Early detection is primarily a function of routine mammography and expert interpretation. In the U.S., a clinical breast examination (CBE) is considered part of the screening process. Clinical breast examination can provide useful information to the radiologic technician and the mammographer concerning areas of the breast that should receive special attention in imaging, or conditions that may suggest alternate techniques of imaging. Practitioners being trained to do CBE frequently use synthetic breast models to simulate examinations. These models are typically representative of relatively dense breasts, and they are modest in size. Opportunities exist to improve the skills of clinicians in examining breasts by making available a wider variety of models that reflect both larger breasts and tissue more typical of post-menopausal women.

Applicants would propose a plan to identify existing models, document gaps, and create models to fill those gaps. Phase two of the proposal would present a plan to market/disseminate the models and evaluate their impact on the practice of CBE.

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### **SKIN CANCER PREVENTION**

One of the most effective ways to reduce the incidence of skin cancer is to protect people from direct exposure to the sun's harmful rays. Encouraging the use of sunscreen, wearing protective hats and clothing, and avoidance of outside activities during certain times of the day are all strategies to change individual behaviors. While such interventions have been implemented with success in some places, it is widely accepted that creating environmental change represents another method of reducing sun exposure.

Evidence suggests that it is cumulative exposure to the sun, and in particular the extent to which sunburn occurs during one's youth, that contribute significantly to the risk of skin cancer. Consequently, many interventions are designed to influence the behaviors of young children or their caretakers. CDC has embarked upon a strategic effort to assist schools to increase their capacity and ability to address sun exposure issues on behalf of the children they serve. Skin cancer guidelines have been developed and are ready for dissemination; a skin cancer module for the "Fit, Healthy and Ready to Learn" curriculum is being prepared.

There is an opportunity for school and community planners to dramatically affect the school environment by ensuring that there is sufficient shade available to protect children while they are outdoors. A guidance document about shade structures and landscaping to create shade around schools is needed. Such a document could also address other recreational areas where children might typically be found, especially during the summer months. Applicants would present a proposal to create a document/tool kit to help schools/sport facilities, pools, parks, and beaches in shade planning and design. Although a document exists that was created by Australia, there is a need to tailor guidance specific to the landscape and environment in the United States.

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## **NATIONAL CENTER FOR ENVIRONMENTAL HEALTH (NCEH)**

The mission of NCEH is to provide national leadership, through science and service, that promotes health and quality of life by preventing or controlling those diseases or deaths that result from interactions between people and their environment.

Research topics include, but are not limited to, those identified below:

- A. **Environmental Health/Anti-Chemical Terrorism—Rapid Field Tests for Human Exposure.** There is a need to develop rapid, reliable, field rugged methods for detection and quantitative estimation of human exposure to environmental contaminants and toxic chemical-based weapons of mass destruction or terrorism. Such methods must be able to sense the presence or absence of such substances quickly and reliably, and provide estimations of concentration in human urine, saliva, breath, blood, or transpired through the skin. Minimums of false positives and false negatives are important for such technology to avoid wasting resources and missing actual exposures.
- B. **Detection of Human Exposure to Aflatoxins and Other Mycotoxins from Food or as Chemical Warfare or Terrorism Agents.** Aflatoxins and other mycotoxins are naturally occurring products of fungi on grains and other food materials. They are produced at harmful levels under certain weather conditions or during improper storage. They have the potential to be weaponized as chemical warfare or terrorism agents. There is a need to develop analytical methods for detection of these compounds in urine, saliva, or blood in the field to support epidemiologic investigations or under battlefield conditions. Methods/instruments must reliably detect and quantify human exposure to these agents, with limits of detection consistent with background levels in populations as well as levels in exposed persons.
- C. **Rapid Field Tests or Continuous Monitors for Arsenic in Drinking Water.** Drinking water with toxic levels of naturally occurring arsenic obtained from shallow wells is a serious problem in many parts of the world. Recently, this problem has become especially acute in rural areas of the under-developed world because of efforts to improve drinking water sources that unfortunately did not fully consider natural sources of arsenic. The solution requires deep wells, or water treatment at the point of use. However, because of uncertainty about the level of arsenic in water from these improved sources, and because of the need to give attention to the most heavily contaminated existing shallow wells first, there is a need to develop rapid, reliable, and cost effective tests or monitors for water arsenic.
- D. **Rapid Field Tests for Iodine Levels in Urine and Salt.** Iodine deficiency is a global problem affecting millions of people, leading to reduced population IQ, cretinism, goiter, and contributing to thyroid cancer. To facilitate efforts to eliminate this problem, rapid, simple, and inexpensive tests are needed that can determine the concentration of iodine in urine for population screening work, and that can determine the concentration of iodine in salt samples for quality control purposes in iodized salt production. While field tests for iodized salt have been developed in recent years, they have proven to be inaccurate and unreliable. Tests for urinary iodine typically have required complicated laboratory procedures. Simple, reliable measures for field use would be a great help.

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### **NATIONAL CENTER FOR HIV, STD AND TB PREVENTION (NCHSTP)**

The mission of NCHSTP is to provide national leadership in preventing and controlling human immunodeficiency virus, other sexually transmitted diseases, and tuberculosis by working with community, state, national, and international partners in effective multi-disciplinary programs of surveillance, research, and evaluation.

#### **Division of HIV/AIDS Prevention**

The Division of HIV/AIDS Prevention provides national leadership through research, policy development, and support of effective programs to prevent HIV infection. We assist health departments, health-care providers, and non-governmental organizations, and collaborate with other governmental entities through research, development, and synthesis of timely, epidemiologically sound information; the development of national goals and policy based on scientific evidence; and transfer of technologies and interventions that have been proven effective, and that meet the needs of the communities affected by HIV.

Develop a training curriculum for teaching persons without any prior laboratory testing the skills necessary to perform point-of-care rapid HIV tests, such as the OraQuick test recently approved by the U.S. Food and Drug Administration, consistent with the NCCLS approved standard for point-of-care testing. The curriculum may be developed in English

or another language (such as Spanish) that would be consistent with the mission of the Division of HIV/AIDS Prevention. The curriculum should be based on state-of-the-art adult learning and education theory, and should be consistent with the NCCLS approved standard for point-of-care testing. The grantee may survey existing materials and develop an educational program suitable for a brief (one-half day or less) educational session. The curriculum may include written, spoken (direct human-to-human interaction), recorded audio, static visual (e.g., posters, leaflets), video, and/or interactive multimedia presentations. Preferably, an interactive curriculum would be suitable for distribution on CD-ROM without the need for additional, specific software. The content should include content on the important phases of testing: patient identification and preparation, specimen collection and performing the test, the recording and reporting of test results and recordkeeping. The curriculum should also be pilot tested to demonstrate comprehension and retention.

#### **Other Research Topic(s) Within the Mission of the Institute**

For technical information on research topics, contact:

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For grants specific information, contact:

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## Division of STD Prevention

The Division of STD Prevention provides national leadership through research, policy development, and support of effective services to prevent sexually transmitted diseases (including HIV infection) and their complications such as enhanced HIV transmission, infertility, adverse outcomes of pregnancy, and reproductive tract cancer. We assist health departments, health-care providers, and non-governmental organizations and collaborate with other governmental entities through the development, synthesis, translation, and dissemination of timely, science-based information; the development of national goals and science-based policy; and the development and support of science-based programs that meet the needs of the communities.

- A. Develop and evaluate a computer software system that provides health care providers (1) computer-based, periodic, confidential, provider-specific feedback about practices for screening young, sexually active women for Chlamydia trachomatis (Ct) and/or screening pregnant women for syphilis; (2) computer-based access to national, state, or local screening guidelines for Ct and/or syphilis; and (3) computer-based continuing education credits to health care providers who demonstrate comprehension of the screening guidelines on Ct and/or syphilis. Evaluation of the provider feedback software system should address acceptability, feasibility, cost, and impact on screening practices.

Dr. Kathleen Irwin

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- B. Develop and evaluate a paper-based medical record flagging system that (1) reminds health care providers during a given primary health care encounter to assess the need to screen that patient for Chlamydia trachomatis (Ct) and/or syphilis given current national, state, or local screening guidelines; and (2) reminds health care providers of the need to offer treatment or additional STD testing to patients with positive Ct and/or syphilis tests. Evaluation of the paper-based chart flagging system should address acceptability, feasibility, cost, and impact on screening practices.

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## Division of NCHSTP/TB Elimination

The mission of the Division of Tuberculosis Elimination (DTBE) is to provide leadership in preventing, controlling, and eventually eliminating tuberculosis (TB) from the United States, in collaboration with partners at the community, state, and international levels.

The mission of the International Activity (IA) of DTBE is to improve the quality of tuberculosis (TB) control programs internationally and among foreign-born in the US, and provide leadership and coordination of CDC activities, in countries with a high burden of TB or having a strategic interest for TB control efforts in the U.S.

- A. Develop a patient education curriculum on tuberculosis (TB) to improve patient adherence to anti-TB treatment in domestic and international settings. The base curriculum may be developed in English or another language that relates to the mission of DTBE. The curriculum should be based on state-of-the-art health communications and education theory and practice. The material may be suitable for multiple sessions or for a single presentation of the materials. The curriculum may include written, spoken (live human to human interaction), recorded audio, static visual (e.g., posters, leaflets), video, and interactive multimedia presentations including CD-ROM or DVD based materials as appropriate. The curriculum should be pilot tested to demonstrate comprehension and retention for each language.

Peter Cegielski, MD;

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- B. Develop a user-friendly computer interface that will enable state and local health departments to create local epidemiological profiles of population groups at high risk for TB for the purpose of targeting TB prevention and control activities. The system would be linked to the Internet and to appropriate supporting software such as database software, statistical analysis software, and geographic information systems. The interface would allow the user to (1) download specific data from public-access, federal data sources. Such sources would or might include the Census Bureau, the National Center for Health Statistics and other Centers of the Centers for Disease Control, the National Association of Health Data Organizations, the

National Association of Public Health Statistics and Information Systems, the Immigration and Naturalization Service, and the Department of Housing and Urban Development; (2) download state TB surveillance data from the nationally standardized Tuberculosis Information System; (3) geocode patient address data available at the state health department to the street address, census block-group, and census tract level; (4) merge the data into a common data base; (5) upload the merged database into one of several standard statistical analysis packages (e.g., SAS, SPSS, Stata); (6) produce tabular and graphic output from automated routines that are generated by a use-friendly point-and-click "front end" user interface; (7) produce point maps and area choropleth maps of the geocoded TB case data; (8) relate these data visually and statistically to thematic maps derived from the other data sources such as demographic and socioeconomic characteristics of the population; and (9) analyze the spatial and temporal distribution of TB cases in relation to the clinical and population data. The goal of the analysis would be to identify specific areas and population groups at high risk for TB, as well as the resources available in terms of social and health services to control the spread of TB and prevent further TB morbidity.

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#### **PUBLIC HEALTH PRACTICE PROGRAM OFFICE (PHPPPO)**

Develop and evaluate a computer software informatics system that (1) includes tools that facilitate and streamline encoding of screening and treatment guidelines in a standard, computable format suitable for dissemination through electronic medical record systems to generate reminders for health care providers during primary health care encounters to assess the need to screen patients for Chlamydia trachomatis (Ct) and/or syphilis according to current national, state, or local screening guidelines; (2) provides ready, computer-based access to national, state, or local screening guidelines for Ct and/or syphilis; and (3) provides health care providers ready, computer-based access to information about how to counsel patients about the benefits and risks of testing and necessary treatment for Ct and/or syphilis and follow up for the

patient and the patient's sex partners in the event of a positive screening test.

Evaluation of the informatics system should address acceptability, feasibility, cost, and impact on screening practices.

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#### **NATIONAL IMMUNIZATION PROGRAM (NIP)**

Applications for SBIR grants from the National Immunization Program should be submitted to the Bethesda, Maryland address indicated in the application materials, but the application form should be marked prominently: "Please forward promptly to CDC, Atlanta, after technical review for funding consideration by that agency"

The National Immunization Program (NIP) of CDC, plans, coordinates, directs, and participates in efforts to prevent and reduce illness and premature death through immunization against disease. Activities include: (1) conducting epidemiology, national surveillance, research and technical consultation on designated diseases for which effective immunizing agents are available, and on the safety of vaccines; (2) assessing immunization levels at national, state, and local levels; (3) guiding the development of recommendations, guidelines, technologies, and policies for effective, safe, efficient, and economical use of existing vaccines, and for the development and incorporation of new and improved vaccines and associated technologies into disease control programs; (4) providing technical, epidemiologic, scientific, statistical, financial, programmatic, and administrative assistance to state and local health departments in support of their immunization programs to prevent diseases recommended for vaccination; (5) implementing national outreach, mobilization, and public information activities to increase understanding about the benefits and risks of vaccines, to promote the demand for them, and to improve immunization practices among health care providers; (6) designing, developing, and implementing information systems to ensure that persons are properly immunized with the recommended vaccines for them; (7) collaborating with the World Health Organization (WHO) and its regional offices and with other CDC Centers/Institutes/Offices (CIOs) in worldwide eradication efforts for polio, and in planning for eradication of other diseases.



### Other Research Topic(s) Within the Mission of the Program

For technical information about the research interests of the National Immunization Program, contact:

Bruce G. Weniger, MD, M.P.H.  
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Vaccine Safety and Development Branch  
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National Immunization Program  
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### NATIONAL CENTER FOR INJURY PREVENTION AND CONTROL (NCIPC)

The National Center for Injury Prevention and Control plans, directs, and coordinates a national program to maintain and improve the health of the American people by preventing premature death and disability and reducing human suffering and medical costs caused by nonoccupational injury, addressing both intentional injuries that result from violent and abusive behavior and unintentional injuries. The national program encompasses the prevention of nonoccupational injuries, and applied research and evaluations in acute care and rehabilitation of injured persons. The Center will address injury prevention and control through an orderly sequence of activities beginning with research on causes, circumstances, and risk factors; progressing through research on interventions and their impact on defined populations. These activities then lead to the broad, systematic applications of interventions that are soundly based scientifically.

CDC is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2010," a PHS-led national activity for setting priority areas. CDC encourages applicants to submit

grant applications with relevance to the specific objectives of this initiative. Potential applicants may obtain a copy of "Healthy People 2010"; (Full Report: Stock No. 017-001-00537-1): through the Superintendent of Documents, Government Printing Office, Washington, D.C. 20402-9325, (202) 512-1800.

More recently, the Centers for Disease Control has published its *CDC Injury Research Agenda*, June 2002, Atlanta Georgia, which identifies 95 research themes in various areas of injury research, including preventing injuries at home and in the community and in sports, recreation and exercise, preventing transportation injuries, preventing intimate partner violence, sexual violence, child maltreatment, youth violence and suicidal behavior and acute care, disability and rehabilitation. The full report is available at <http://www.cdc.gov/ncipc>.

The focus of the research topics for SBIR should reflect the themes represented in the research agenda designed to control injury, morbidity, mortality, disability, and costs. These projects may be categorized by the three phases of injury prevention and control. Research topics of interest include, but are not limited to:

A. **Prevention.** There is interest in the development, application, and evaluation of innovative interventions applicable to intentional and unintentional injury. The focus should reflect target populations at high risk for injury and injury consequences, including minorities, children, the elderly, rural residents, and farm families. SBIR projects that have relevance for reducing injury or increasing dissemination and adoption of effective injury prevention interventions are sought. The following are examples:

1. Develop improved smoke alarm technology (e.g., smoke alarms with a lower audible frequency for those with high-end hearing loss; smoke alarms with more accurate detection for dangerous levels of smoke and dangerous particulate matter, less intrusive self-testing devices, increased coverage radius, etc.
2. Develop a practical, valid screening tool to assess an older driver's fitness to drive safely, or walk safely in traffic as a pedestrian, taking into account mental, perceptual-motor and physical/medical condition.

3. Develop devices that help alert drowsy and distracted drivers and prevent inattention that contributes to motor vehicle crashes.
4. Design, develop, and evaluate educational materials to train public health personnel in injury prevention that could be adapted for medicine, nursing and allied health.
5. Develop and evaluate injury and violence prevention materials uniquely targeted to and disseminated in medical care and managed care settings, such as in-house kiosks, computer-based self-assessments, and clinical preventive services based interventions or through the use of distance-based learning technology. These materials can address topics such as falls, helmets, supervision and prevention of youth violence or intimate partner violence.
6. Design and develop innovate scald prevention devices.
7. Design and develop improved and effective driver and motorcycle training programs for beginning drivers.
8. Design, develop and evaluate a garment with hip protector that is acceptable to the public, comfortable and effective in preventing a hip fracture in older adult women during a fall.
9. Develop and test a passive alcohol sensor device to passively measure the blood alcohol level of injured patients arriving at the emergency department.
10. Design and test a home-based program to assist teens and their parents to manage "graduated licensing" requirements for new teen drivers.
11. Design and develop a safe device to deter dog attacks.
12. Develop improved sensors for cars that will improve visibility of drivers in heavy fog, rain, or snow.
13. Develop, test, and evaluate devices that will reduce deaths and suffocations of children left in cars unattended.
14. Develop and test methods to improve the occupant protection of women driving or riding in automobiles, light trucks, and vans.

15. Design and develop academic instructional materials on injury and violence prevention for grades K through 12 that can be integrated into comprehensive school health education.

**B. Acute Care.**

1. Develop developmentally appropriate devices, instruments, methods, models, tests, and computer software related to the full spectrum of acute care of the trauma patient, beginning with the establishment of access to emergency care, response at the injury scene, transportation of the critically injured, to management of postoperative complications such as multiple organ failure syndrome.
2. There is a need to improve diagnostic modalities in several areas, particularly in those related to perfusion and oxygenation at the tissue level. Further, among those patients whose bleeding has been controlled and who will survive the acute phase of injury, the major causes of death are irreversible cerebral damage or uncontrollable cerebral swelling and multiple organ failure. There is an urgent need for research into methods of reducing secondary cerebral injury and of controlling brain swelling and preventing multiple organ failure.
3. Design, develop and evaluate Emergency Department-based prevention services for the identification and referral of persons at risk for violence or alcohol-related injury.

**C. Rehabilitation.**

1. Develop developmentally appropriate adaptive equipment, assistive devices, and instructional materials directed toward preventing or minimizing the secondary complications of individuals with traumatic brain or spinal cord injuries including cognitive learning problems, pressure ulcers, contractures, muscular atrophy, skeletal deformity and other definable conditions.
2. Design, develop and evaluate educational materials for persons with traumatic brain or traumatic spinal cord injury, their families and/or caregivers that are directed toward preventing or minimizing the secondary complications associated with these injuries.

3. Develop training materials to assist persons with disabilities and their care givers to safely and efficiently evacuate various buildings, (e.g., multi-storied structures) in emergencies.

### Other Research Topic(s) Within the Mission of the Center

For programmatic information, contact:

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For grants specific information, contact:

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### FOOD AND DRUG ADMINISTRATION (FDA)

**FDA will now accept SBIR grant applications on the same schedule as NIH—April 1, August 1, and December 1, 2003.**

The mission of the Food and Drug Administration (FDA) is to protect the public health of the Nation as it may be impaired by foods, drugs, biological products, cosmetics, medical devices, ionizing and non-ionizing radiation-emitting products and substances, poisons, pesticides, and food additives. FDA's regulatory functions are geared to insure that

foods are safe, pure, and wholesome; drugs, medical devices, and biological products are safe and effective; cosmetics are harmless; all of the above are honestly and informatively packaged; and that exposure to potentially injurious radiation is minimized.

For additional information about areas of interest to the FDA, please visit our home page at <http://www.fda.gov>.

### CENTER FOR BIOLOGICS EVALUATION AND RESEARCH (CBER)

CBER is responsible for ensuring the safety, efficacy, potency and purity of biological and related products intended for use in the treatment, prevention or cure of diseases in humans as well as the safety of the nation's supply of blood and blood products. The primary responsibility of CBER is to review the quality, safety and efficacy of vaccines, blood products, certain diagnostic products and other biological and biotechnology-derived human products.

CBER's activities include: evaluating the quality, safety and effectiveness of biological products before marketing, and monitoring the pre-clinical and clinical testing of new biological products; licensing biological products and manufacturing establishments, including plasmapheresis centers, blood banks, vaccine and biotechnology manufacturers; AIDS program and policy activities, including research on AIDS therapeutic products, diagnostic tests and vaccines; research to establish product standards, develop improved testing methods and assess the safety of biological products; compliance, lot release program and post market surveillance; meeting PDUFA goals, new research programs, and new regulatory initiatives (managed review process for all products).

### CENTER FOR DRUG EVALUATION AND RESEARCH (CDER)

CDER develops FDA policy with regard to the safety, effectiveness, and labeling of all drugs for human use; evaluates new drug applications and investigational new drug applications; develops standards for the safety and effectiveness of all over-the-counter drugs; monitors the quality of marketed drugs through product testing (bioavailability/bioequivalence testing), post marketing surveillance, and compliance programs; develops guidelines on good manufacturing

practices; conducts research and develops scientific standards on composition, quality, safety, and efficacy of human drugs.

Drug regulatory research as conducted in CDER is directed at the discovery of new knowledge relevant to drug development, postmarketing drug experience (patterns of drug use and safety), and drug regulation to enhance FDA regulatory decisions. These drug regulatory decisions impact on the development of regulations, guidelines and guidance for the regulated industry and provide clarity and consistency in application of CDER regulatory requirements. These drug regulatory decisions also impact public health by ensuring that marketing drugs are safe and efficacious and that their risk: benefit profile remains acceptable during the market life of a drug. Specific areas of research conducted by the Center include:

Pharmacology/toxicology, microbiology/virology, clinical pharmacology, pediatric issues in drug therapy, postmarketing drug safety, evaluation of effectiveness of regulatory actions, patterns of drug use, including off-label, signal detection methodologies (e.g., datamining techniques), epidemiologic studies of therapeutics using population-based data, regulatory compliance, product quality, and active surveillance methods.

Research and development opportunities within the FDA that lend themselves to performance by small businesses include, but are not limited to, the following:

- A. Develop a system for gathering real-time data on physician prescribing behavior, understanding and compliance with drug product labeling and frequency of off-label prescribing.
- B. Develop and evaluate the effectiveness of new methods and tools for managing the known risks of marketed drug products (e.g., communicating newly identified risks to health care practitioners and patients).
- C. Develop methods for timely active surveillance of newly approved drug products in large populations to identify both expected and unexpected outcomes.
- D. Develop methods for actively collecting information on all cases of classically drug-associated events (e.g., acute liver failure, blood dyscrasias, severe desquamating skin disorders) to augment the FDA's current passive surveillance system.

- E. Develop improved clinical markers and methods with potential for bed-side application for detection of the early onset of adverse drug events.
- F. Develop surrogate potency methods for biotech drug products to replace traditional animal testing.
- G. Development of psychochemical and in-vitro biological tests to evaluate pharmaceutical equivalence of complex drug substances and drug products.

### **CENTER FOR FOOD SAFETY AND APPLIED NUTRITION (CFSAN)**

The Center for Food Safety and Applied Nutrition conducts research and develops standards on the composition, quality, nutrition, and safety of food, food additives, colors, and cosmetics. The Center also evaluates FDA's surveillance and compliance programs relating to foods, colors, and cosmetics; reviews industry petitions and develops regulations for food standards to permit the safe use of color additives and food additives; collects and interprets data on nutrition, food additives, and environmental factors affecting the total chemical result posed by food additives; and maintains a nutritional data bank.

The Center is mindful that as a leader in food safety, communicating our needs to other agencies and to its partners in academia and industry is critical to the achievement of our regulatory mission. As part of the CFSAN's research planning process, we have developed a list of priority research needs. CFSAN seeks research designed to complement and accelerate efforts for the detection, prevention, and control of contamination that may be responsible for illness or injury conveyed by foods, colors, and cosmetics. The complete list of the Center's priority research needs can be viewed at <http://www.cfsan.fda.gov/~dms/resneeds.html>. We will be happy to provide more information on any of the research areas identified and to meet with representatives from industry and academia that are interested in learning more about the Center's research priorities.

### **CENTER FOR DEVICES AND RADIOLOGICAL HEALTH (CDRH)**

CDRH develops FDA policy and solves problems related to public health and safety of medical devices and radiation-emitting electronic products. It

evaluates applications for premarket approval of medical devices, approves products development protocols and exemption requests for investigational devices. It classifies devices into regulatory categories, develops safety and effectiveness standards and good manufacturing practices regulations, operates postmarket surveillance and compliance programs, and provides technical, non-financial assistance to small manufacturers. The Center also conducts programs to reduce human exposure to hazardous ionizing and nonionizing radiation, through an electronic product radiation control program and other programs designed to control and to limit radiation exposure. The Center develops and conducts research and testing programs in the areas of physical, life, and engineering sciences related to the human health effects of radiation and medical device technologies, provides expertise and analyses for health-risk assessments, and also develops new or improved measurement methods, techniques, instruments and analytical procedures for evaluating product performance and reliability. The overall research program may be categorized into four areas, as follows:

1. Characterization of the constituents or components of products.
2. Measurement of product performance.
3. Bioeffects that derive from human exposure to radiation or medical devices.
4. Radiation metrology in support of Agency regulation of radiation-emitting products.

Research and development opportunities within the FDA that lend themselves to performance by small businesses include, but are not limited to, the following:

- A. Develop an optical non-destructive method for rapid microtopographic evaluation and measurement of wear of articulating surfaces of implant prostheses.
- B. Develop a system, including CDROM database of human chemical physiological, electrical and mechanical service environment test parameters, for use to design test protocols for implant device performance and for accelerated reliability testing.
- C. Develop a system, including database and radiation dosimetry badges, for monitoring and registering radiation exposure (dose) of health care providers during interventional radiologic

procedures (e.g., angioplasty, percutaneous renal stone removal).

- D. Perform human factors analysis of design and operation of one or more medical devices such as infusion pumps, defibrillators or endoscopes.

### **CENTER FOR VETERINARY MEDICINE (CVM)**

CVM is a public health organization that enables the marketing of effective drugs, food additives, feed ingredients, and animal devices that are safe to animals, humans, and the environment. The Center, in partnership with Federal and state agencies and other customers, ensures animal health and the safety of food derived from animals. The Center makes timely, quality decisions and takes regulatory actions to ensure that these products provide for quality health care of animals, minimize the transmission of zoonotic diseases, and increase the efficiency of production of animal-derived food and fiber. Regulatory decisions are supported by research, the monitoring of product safety, and efficacy, and the continual improvement of processes.

### **OFFICE OF ORPHAN PRODUCTS DEVELOPMENT**

The Office of Orphan Products Development was established to identify and facilitate the development of orphan products. Orphan products are drugs, biologics, medical devices and foods for medical purposes, which are indicated for a rare disease or condition (i.e., one affecting fewer than 200,000 people in the United States). These products may be useful in a rare disease/disorder but lack commercial sponsorship because they are not considered commercially attractive for marketing. A subcategory of orphan products are those marketed products in which there is evidence suggesting usefulness in a rare disease/disorder but which are not labeled for that disease/disorder because substantial evidence of safety and effectiveness for that use is lacking.

Research and development opportunities within the FDA that lend themselves to performance by small businesses include, but are not limited to, the following:

- A. Development of pediatric formulations for already approved products for the specific purpose of submitting data to the FDA to

include pediatric labeling to the current label of the approved product.

- B. Development of products for the treatment of rare diseases or disorders including but not limited to neurological, metabolic, genetic, ophthalmologic, hematologic, and dermatological diseases or disorders for the specific purpose of obtaining marketing licensure.
- C. Development of products for use in diagnosis of rare diseases for which the diagnostic tool would be used in fewer than 200,000 persons annually in the United States.
- D. Development of vaccines for the prevention of rare diseases to be used in fewer than 200,000 persons annually in the United States.

#### **Other Research Topic(s) Within the Mission of FDA**

For additional information on research topics and administrative and business information, contact:

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